



Clinical Urology

BY

OSWALD SWINNEY LOWSLEY

A.B., M.D., F.A.C.S.

*Director of the Department of Urology (James Buchanan Brady Foundation)
of the New York Hospital*

AND

THOMAS JOSEPH KIRWIN

M.A., M.S., M.D., F.A.C.S.

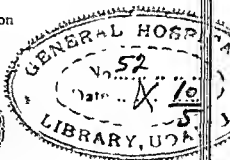
*Attending Surgeon of the Department of Urology (James Buchanan Brady
Foundation) of the New York Hospital*

DRAWINGS BY

WILLIAM P. DIDUSCH

Second Edition

Volume II



Baltimore

THE WILLIAMS & WILKINS COMPANY

1944

COPYRIGHT, 1944
THE WILLIAMS & WILKINS COMPANY

Made in the United States of America

First Edition, September, 1940

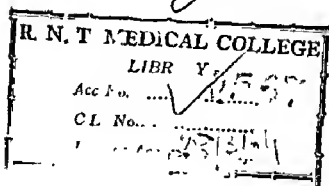
Reprinted December, 1941

Second Edition, February, 1944

Reprinted July, 1944

Reprinted July, 1946

2567



COMPOSED AND PRINTED AT THE
WAVERLY PRESS, INC.
FOR
THE WILLIAMS & WILKINS COMPANY
BALTIMORE MD., U. S. A.

CONTENTS OF VOLUME II

CHAPTER XXX

EMBRYOLOGY, ANATOMY, ANOMALIES, AND PHYSIOLOGY OF THE BLADDER

Embryology of the bladder	943
Anatomy of the bladder	946
Anomalies of the bladder ..	957
Physiology of the bladder .	968

CHAPTER XXXI

INJURIES AND DISEASES OF THE BLADDER

Injuries to the bladder	986
Diseases of the bladder.....	994

CHAPTER XXXII

OPERATIVE AND NON-OPERATIVE TREATMENT OF THE BLADDER

Operative treatment of the bladder.	1102
Non-operative treatment of the bladder	1158

CHAPTER XXXIII

EMBRYOLOGY, ANATOMY, ANOMALIES, AND PHYSIOLOGY OF THE URETER

Embryology of the ureter	1208
Anatomy of the ureter	1210
Anomalies of the ureter	1213
Physiology of the ureter	1226

CHAPTER XXXIV

INJURIES AND DISEASES OF THE URETER

Injuries to the ureter	1232
Diseases of the ureter	1239

CHAPTER XXXV

OPERATIVE TREATMENT OF THE URETER

Preoperative preparation	1302
Preparation of the operative field	1302
Anesthesia	1302
Surgical treatment of ureteral anomalies	1302
Surgical treatment of stenosis of the ureterovesical orifice ...	1304
Surgical treatment of non-calculous obstructions at the ureteropelvic junction.....	1305
Operative treatment of ureteral injuries.....	1315
Operative treatment of ureteral calculus ..	1320
Ureterectomy	1324
Uretero-intestinal anastomosis ..	1324

CHAPTER XXXVI

EMBRYOLOGY, ANATOMY, ANOMALIES, AND PHYSIOLOGY OF THE KIDNEY

Embryology of the kidney.	1343
Anatomy of the kidney	1350
Anomalies of the kidney	1361
Physiology of the kidney	1384

CHAPTER XXXVII

INJURIES AND DISEASES OF THE KIDNEY

Injuries of the kidney and renal pelvis	1395
Diseases of the kidney and renal pelvis	1405

CHAPTER XXXVIII

OPERATIVE AND NON-OPERATIVE TREATMENT OF THE KIDNEY

Operative treatment of the kidney	1655
Non-operative treatment of the kidney	1715

CHAPTER XXXIX

RADIUM AND ROENTGEN-RAY THERAPY OF THE GENITO-URINARY TRACT

Introduction	1724
Carcinoma of the penis	1734
Epithelioma of the scrotum	1736
Tumors of the testicle	1736
Malignant tumors of the seminal vesicle and spermatic cord	1739
Malignant tumors of the female external genitalia	1739
Malignant tumors of the male urethra	1742
Malignant tumors of Cowper's glands	1743
Malignant tumors of the female urethra	1744
Radiation treatment of benign hypertrophy of the prostate gland	1745
Carcinoma of the prostate gland	1747
Tumors of the bladder	1750
Tumors of the kidney and ureter	1758

CHAPTER XL

DRIED HUMAN BLOOD PLASMA THERAPY

Preparation and packaging of dried plasma	1766
Advantages of plasma over whole blood	1767
Dangers of plasma administration	1768

INDEX	i
-----------------	---

CHAPTER XXX

EMBRYOLOGY, ANATOMY, ANOMALIES, AND PHYSIOLOGY OF THE BLADDER

The urinary bladder is an unpaired musculomembranous sac which serves as a reservoir for the urine. Into its lower and posterior portion the ureters empty, and from its neck the urethra arises.

A. EMBRYOLOGY OF THE BLADDER

The human bladder is derived almost wholly from the entodermal cloaca. A small portion, the *trigonum vesicae*, arises from the inclusion of the proximal ends of the mesonephric ducts, and is, therefore, of mesodermal origin.

The Primitive Cloaca. In very young embryos the hindgut and the allantois unite in a common *cloaca*, which is for a time shut off from the external surface of the embryo by the *cloacal membrane*, formed by the apposition of the ectoderm and entoderm. Into the dorsal part of the cloaca the hindgut opens, and from its ventral portion the allantois extends outward into the body stalk. At a somewhat later stage (about 4 mm.) the mesonephric ducts open into its dorso-lateral walls.

Subdivision of the Cloaca. In embryos of 5.3 mm. the cloaca becomes divided, by the downward growth of the *urorectal septum*, into two parts: the dorsal *rectum* and the larger, ventral *primitive urogenital sinus*. The septum starts to grow in the angle between the allantois and the hindgut, and proceeds caudally until it fuses with the cloacal membrane, separating the latter into two portions: the *anal membrane* and the *urogenital membrane*. Subsequently (between 13 and 18 mm.) the anal and urogenital membranes become perforate.

The Vesico-urethral Anlage. At about 11 mm., the primitive urogenital sinus, by elongation and constriction, subdivides into two parts: (1) a dorsal *vesico-urethral anlage*, which receives the allantois and mesonephric ducts and is connected by a narrow neck—the *pars pelvina*—with (2) a ventral portion, the *pars phallica of the urogenital sinus*. From the vesico-urethral anlage (which enlarges and receives the mesonephric ducts and the associated ends of the ureters) is formed

the bladder and the posterior urethra in the male; in the female, the bladder and practically the entire urethra are formed here. The phallic segment extends into the genital tubercle of both sexes, developing into the cavernous urethra in the male but merging with the vestibule in the female. The development of the urogenital sinus has been considered elsewhere.

The ureteral bud appears, at 6 mm., as a localized thickening at the sagittal bend made by the mesonephric duct before it reaches the cloaca. At first it grows laterally, but at 9 mm. it has turned and is growing cranially, and at 10 mm. it has reached the mesonephric duct.

The mesonephric ducts at first open into the latero-dorsal wall of the vesico-urethral anlage, but, with subsequent development, their proximal ends become dilated (at 10 mm.) and, with the enlargement of the bladder, these ends are taken up into the walls of the vesico-urethral segment. During this process of absorption the ureters (which originally opened on the dorsal walls of the mesonephric ducts) acquire separate openings into the vesico-urethral anlage lateral to the orifices of the mesonephric ducts. This absorption of the ends of the mesonephric ducts and the associated ends of the ureters gives rise to the trigone of the bladder and part of the prostatic urethra, which are, therefore, of mesodermal origin. The lateral walls of the bladder anlage grow more rapidly than its dorso-median (urethral) wall; hence the ureteral orifices are carried cranially and laterally to their final positions, while the mesonephric ducts, which ultimately become the ejaculatory ducts, retain their original caudad position, opening close together upon Müller's tubercle (the early verumontanum) in the dorsal wall of the posterior urethra.

The allantoic duct, which opens into the cranial end of the bladder, degenerates into a solid epithelial cord—the urachus—which extends from the vertex of the bladder to the umbilicus and becomes the medial umbilical ligament. Occasionally the urachus may form, after birth, a patent tube opening at the umbilicus.

Development of the Trigonum Vesicae. The trigone of the bladder is a smooth, triangular area situated in the base of the viscus, having the two ureters and the vesical orifice at its angles. It consists of the two muscle layers of the bladder wall—the external longitudinal and the middle circular—upon which are superimposed the trigonal muscle, which is an expansion of the longitudinal muscle fibers of the ureteral wall.

Unlike the rest of the bladder, which is of entodermal origin, the trigone is derived from the mesoderm. As we have seen, it is developed from the walls of the mesonephric ducts, the terminal portions of which, by a process of absorption, are taken up, with the proximal ends of the ureters, into the wall of the primitive bladder. The cranio-lateral migration of the ureters, which begins at the 13-mm. stage, causes the area between the ureteral orifices and Müller's tubercle (containing the openings of the mesonephric ducts) gradually to assume a triangular form. Wesson found that in the 21-mm. embryo the trigone forms an equilateral triangle each side of which measures 0.36 mm. A transverse section of the bladder at this stage presents an appearance similar to a half moon; and while this investigator found that occasionally the ureters entered at the tips of the half moon, as described by most embryologists, in the majority of cases they entered on the dorsal aspect, about 0.03 mm. from the tips. At 80 mm. the ureters enter the bladder in an oblique direction.

Epithelium and Musculature. The transitional epithelium of the bladder appears in embryos of about 60 mm. In very early embryos the primitive vesico-urethral tract is lined by a single layer of cylindrical epithelium. New layers are added from the 13 to 60-mm. stage. At 40 mm. the epithelium of the trigone consists of four or five layers, while that of the remainder of the bladder is composed of two layers.

A condensation of loose mesenchyme tissue precedes the formation of the musculature. The first muscular layer is seen to develop as a longitudinal layer (at 20 mm.) and extends from the bladder apex almost to the ureteral orifices. Next to develop is the circular layer (at 26 mm.) and lastly the inner longitudinal layer (at 55 mm.). The sphincter vesicae does not attain its mature form until the embryo is about 90 mm. long (in the fourth month).

At 30 mm. (10 weeks), the bladder is a tubular structure which narrows down gradually as its orifice is approached. The site of the future vesical sphincter is indicated only by change in the size and shape of the lumen. The wall is uniform in thickness everywhere except in the region of the trigone, where it is nearly twice as thick as at any other point. Connective tissue strands can be traced from the ureters out into the trigone, the trigone itself being quite definitely superimposed upon the vesical wall. General thickening is perceptible throughout the bladder base but is particularly noticeable in the interureteral area.

At 70 mm. (thirteenth week), this thickening of the trigonal region is

much more marked. The musculature of the embryonal bladder can now be distinctly recognized as a deeper staining tissue composed of interlacing circular and longitudinal strands, which are easily differentiated from the connective tissue elements still forming the major portion of the bladder wall. The strands of muscle tissue are much larger and more abundant throughout the entire base of the bladder than in the remainder of its circumference, while the trigone is five times as thick as the remaining portion of the wall. The embryonal differences between it and the rest of the bladder are always in evidence. The muscular strands of which it is composed are much finer in texture than those found elsewhere, and may be traced between the two ureters and so out into other portions of the trigone.

By the sixteenth week the muscular fibers of the bladder wall are sufficiently developed to be sharply defined from the surrounding connective tissue, and it is easy to trace from the ureteral walls the muscular fibers forming the trigone. The mucosa of the trigone is smooth, although elsewhere it lies in folds. By the twentieth week there is an enormous increase in the size and number of the fibers forming the vesical sphincter. Development of the bladder musculature goes steadily forward as growth continues, the base being always the thickest part.

B. ANATOMY OF THE BLADDER

Position. The bladder in the adult is practically a pelvic organ, rising into the abdomen only when distended. In fetal and infantile life it is mostly abdominal, the internal urethral orifice lying on a level with the upper edge of the symphysis pubis; but during the first two decades of life it gradually descends, reaching complete descent in both sexes in about the twentieth year.

In the female, the bladder is more anterior than in the male on account of the uterus. It also lies somewhat lower in the pelvis—the position of the prostate and the greater length of the urethra necessitating higher placement of the bladder in the male.

Shape: Attachments: Relation to Adjacent Structures. The shape of the bladder depends upon the degree of distention, the nature of its attachments, and its relation to adjacent structures. When empty, it has the form of a cone, in the male, with the vertex directed toward the upper part of the symphysis pubis; in the female, it is more extended in the transverse direction and is usually flattened from above. When full, it is egg-shaped, the long diameter being directed upward and forward

The bladder is in part an extraperitoneal organ. Its postero-superior surface is covered with peritoneum and is free and distensible; but its antero-inferior surface and the lower part of the lateral surfaces are devoid of peritoneum. The space between the anterior surface of the bladder and the symphysis pubis and transversalis fascia, occupied by areolar tissue, is known as the *prevesical space* or *space of Retzius*. Its upper limit is marked by the urachus, and postero-laterally it extends as far back as the rectum. This space is of great importance surgically because it permits easy mobilization of the bladder when necessary and because it is very easily infected during operation.

In the male, the bladder is situated between the symphysis pubis and the rectum. The anterior surface lies just behind the symphysis and the neighboring parts of the pubic bones, from which it is separated above by areolar tissue only, and below by areolar tissue, the pelvic fascia, and the vesical plexus. The inferior surface, which is uncovered by peritoneum, adjoins the base of the prostate. From it the urethra emerges. The posterior surface is in relation with the seminal vesicles, the ampullae of the vasa deferentia, and the rectum, being separated from the last by the rectovesical pouch.

In the empty bladder only the superior surface is directly covered by the peritoneum. The infero-lateral surfaces are entirely devoid of peritoneum. When the bladder fills, it rises into the hypogastric region. Therefore, the peritoneal reflexion from the apex is raised along with the organ, and, as a result, a considerable area of the bladder wall below the urachus (ligamentum umbilicæ medium) becomes applied directly to the anterior wall, with no peritoneum intervening. When there is retention of urine, and a catheter can not be passed, the bladder may therefore be punctured immediately above the symphysis pubis without fear of injuring the peritoneum.

In the female, the bladder lies between the symphysis pubis and the uterus. It rests upon the anterior wall of the vagina, and is connected with it and the cervix uteri by areolar tissue rich in veins. It is separated from the anterior surface of the body of the uterus by the uterovesical pouch.

The bladder is held in position by means of the prostate and urethra at the neck, the rectovesical (in the female, uterovesical) pouch behind, and by so-called *true ligaments* and *false ligaments*. The true ligaments are reflections of the pelvic fascia: the *anterior true ligament* or *pubo-prostatic ligament*, which extends from the back of the pubic bones to

the anterior part of the bladder and prostate, and the *lateral true ligaments*, reflections of the pelvic fascia from the levator ani muscles onto the bladder at its upper portion. Extending upward from the vertex, to the umbilicus, and forming a *superior ligament*, is a fibromuscular cord, the *medial umbilical ligament*, which represents the remnant of the obliterated embryonic urachus. The *false ligaments* are simply reflections of the peritoneum which form vesical connection with the walls of the pelvis and abdomen.

Size. When moderately distended, the normal adult bladder contains approximately 500 cc. (1 pint). The capacity varies considerably and it is capable of great distention without rupture.

Structure of the Bladder Wall. The bladder wall is composed of four coats: *serous*, *muscular*, *submucous*, and *mucous*.

The *serous coat* is a partial one. It is derived from the peritoneum and, as we have seen, invests the postero-superior surface and the upper parts of the lateral surfaces, from which it is reflected onto the abdominal and pelvic walls.

The *muscular coat*—*detrusor vesicae*—consists of three imperfectly defined layers of loose interlacing bundles of unstripped muscular fibers: an external longitudinal layer, a middle circular layer, and an incomplete internal layer of very delicate longitudinal fibers loosely arranged within the submucosa. The muscular coat is stronger at the base and weaker and more net-like above, where distention occurs. All three layers are intimately connected with one another since bundles from one go over into the others. The direction of the fibers and the number of layers into which they can be separated varies with the degree of distention, as the muscle fibers rearrange themselves during dilatation and contraction of the bladder.

The *submucosa*, present everywhere except over the trigone, is a vascular areolar tissue with abundant elastic fibers. It connects the muscular and mucous coats and is intimately united to the latter.

The *mucosa* is thin, of a pale rose color, and continuous with the mucosa of the ureters above and the urethra below. Over the greater part of the bladder it is loosely attached to the muscular coat by the submucosa, and lies in folds when the bladder is empty. In the distended state the folds disappear. Over the *trigonum vesicae* the mucous membrane is intimately attached to the underlying muscular coat and is always smooth and flat. The mucosal epithelium is of the transitional variety. The cells are of various sizes and shapes and, in the contracted state,

are arranged in several layers which flatten out into one or more layers when the bladder is distended. There are no true glands in the bladder mucosa, although certain mucous follicles, present particularly in the region of the vesical neck, have been so regarded.

Interior of the Bladder. The postero-inferior portion of the bladder, directed toward the perineum, contains the vesical orifice and the trigonum vesicae. The remainder is called the *body of the bladder*.

The *vesical orifice* (internal urethral orifice) is the most dependent portion of the bladder. When closed, it is shaped like an inverted crescent in men; in women, it is more circular. During micturition it is triangular in both sexes, as the result of the contraction of the trigonal muscle at the base and the synchronous relaxation of the two loops of muscle about the orifice.

The *trigonum vesicae* is a smooth, triangular area at the base of the bladder, and stands out markedly from other portions of the viscus. It is closely related to the vesical neck and to the prostatic urethra. Its anterior angle, or apex, is formed by the internal orifice of the urethra; its postero-lateral angles by the slit-like orifices of the ureters, which are usually about 2.5 cm. (1 inch) apart and about the same distance from the internal urethral orifice in the undistended bladder. Stretching between the ureteral orifices is a fold or ridge—the *interureteral ridge* (Mercier's bar; median bar)—which, with the ureteral orifices, marks the base of the trigone. The ureters pierce the bladder wall obliquely, and each orifice presents a small fold—the *ureteral ridge*. The shape and size of the trigone display great individual variations independent of age, sex, or the size of the bladder. The size of the ureteral orifices, and their relation to the interureteral ridge, also vary considerably. The *uvula vesicae* is a small, median, longitudinal projection at the apex of the trigone, being continuous with the verumontanum. The mucous membrane of the trigone differs from that of the remainder of the bladder in its deeper color and in that it is firmly attached to the underlying musculature and is smooth and free of folds. Subtrigonal glands occur commonly, lying between the vesical orifice and the middle of the trigone. As a rule, they are simple tubules lying in the mucosa, without fibrous envelops, but occasionally they may have one or two small branches and extend into the muscle layer. They are of little clinical importance unless they hypertrophy and cause obstruction to urination.

The *bas-fond* or *postprostatic pouch* is the depressed area in the posterior wall just behind and above the trigone. It enlarges in prostatics

and then contains retained urine. It is also a favorite lodging-place for calculi.

The Bladder Musculature. The bladder wall contains three groups of muscle fibers which, with the external sphincter (sphincter urethrae) and the accessory urethral and perineal muscles, form the musculature of micturition (Physiology of the Bladder, p. 968). These muscular structures are (1) the *detrusor vesicae*, (2) the trigonal muscle, (3) the internal "sphincter."

The Detrusor Vesicae. *Detrusor vesicae* is the term used to denote the entire thickness of the muscular coat of the wall. The detrusor is the most powerful muscle concerned in micturition. It is composed of three imperfectly defined layers of unstriated muscle—an external longitudinal, a middle circular, and an incomplete internal longitudinal—which are so interwoven that they really constitute a functional unit. The middle circular is the strongest and most complete layer. The detrusor is attached to the back of the symphysis pubis and to its own fibromuscular arrangement at the vesical neck, which, in turn, is attached to the base of the prostate in the male and to the upper part of the urethra in the female.

The *external longitudinal* layer consists of rather coarse bundles of fibers arranged more or less longitudinally. As they approach the vesical orifice, the longitudinal fibers converge into relatively narrow bands on both the anterior and posterior surfaces. The *posterior band of longitudinal fibers* passes between the ureters and forms a very definite tract. Most of the fibers pass forward between the prostate and the bladder mucosa, and diverge slightly to form two muscular bands which pass forward and downward on either side of the urethra and then, at the upper level of the urethra, swing medially to form a loop about the urethra. Together with striated muscle fibers of this region, with which they blend, these fibers form the *external urethral loop* (external arcuate muscle of Young and Wesson; external vesical sphincter of Henle and McCrea). In the male, some of the fibers from the posterior longitudinal band become lost in the prostate; others terminate in the circular fibers of the vesical neck; while still others pass vertically downward within the ring of the external urethral loop to unite with the submucosal layer of the urethra. In the female, certain fibers from the posterior band pass downward into the posterior wall of the urethra. Most of the longitudinal fibers sweeping down the *anterior* surface of the bladder terminate at the vesical neck in the fibromuscular *detrusor ring*. A few

sweep laterally away from the bladder neck and become attached to the posterior aspect of the pubes; a few follow the course of the circular fibers; while others continue downward on the anterior aspect of the prostatic urethra to form an internal longitudinal layer of the urethra.

The *middle circular* layer is composed of coarse muscular bundles circularly arranged for the most part and of considerable thickness except in the trigonal region. About the point of entry of the ureter the circular fibers diverge and a Y-shaped structure results, the stem of the Y lying inferiorly and the ureter entering between the limbs of the Y. As the base of the bladder is approached, the bundles passing anteriorly from the stem of the Y on either side are especially well marked and compact (McCrea).

The detrusor vesicae is innervated by the pelvic nerves (parasympathetic) from the sacral portion of the cord and by the hypogastric nerves (sympathetic) from the thoracolumbar portion of the cord (Innervation, p. 969).

The Trigonal Muscle. The trigonum vesicae, as already described, is a smooth, triangular area lying at the base of the bladder, its angles being marked by the two ureteral orifices above and the internal urethral orifice below, at the apex. Two layers of the detrusor—the external longitudinal and the middle circular—enter into the formation of the trigone. Superimposed upon these is the *trigonal muscle*, which is a definite entity, and is actually an expansion of the longitudinal muscle fibers of the walls of the ureters. Its fibers extend fanwise from the ureteral orifices: some, passing medially, form the interureteral ridge which marks the upper boundary of the trigone; others interlace with those from the opposite side in the middle of the trigone; and still others pass downward to the vesical orifice, forming the ureteral ridges (Bell's muscles). As Bell originally pointed out, these two muscles converge at the vesical orifice, causing the trigonal muscle at this point to be greatly thickened. The fibers pass through the vesical orifice and continue downward along the urethra, thinning out to form an internal longitudinal layer on the posterior aspect of the prostatic urethra.

Behind the interureteral ridge the circular layer of the detrusor is formed of large, loose bundles of muscle fibers, but as it passes beneath the median bar the bundles become smaller and more compact. The longitudinal bundles also become more compact as they pass under the trigone to the vesical orifice. These longitudinal bundles are surrounded by elastic fibers which, when the muscle terminates, persist and pass on

through the circular layer to disappear at its upper edge. These fibrils, Wesson believes, may form an attachment or tendon for the muscle fibers which end in this region.

The rounded eminence at the apex of the trigone—the *uvula vesicae*—is formed by the submucosal convergence of many muscular fibers as they pass through the detrusor ring.

The trigonal muscle is innervated by the sympathetic fibers of the hypogastric nerves only, while the bladder wall has sympathetic and parasympathetic fibers.

The Internal "Sphincter." The internal "sphincter" (sphincter vesicae), unlike the external sphincter (sphincter urethrae), is not a simple annular muscle constricting the vesical orifice, but an exceedingly complex arrangement that has given rise to much study and controversy. To date, however, the disputes regarding its details of structure and mechanism of activity have not been fully reconciled. Outstanding among the contributors to this subject have been Young and Wesson (1920) and McCrea (1926).

(Young and Wesson's Theory.) The theory of Young and Wesson is that the vesical orifice is closed by two loops or arcs, one—the *external arcuate muscle of the vesical orifice*—arising from the external longitudinal layer of the detrusor vesicae, and the other—the *internal arcuate muscle of the vesical orifice*—arising from the middle circular layer of the detrusor. Their investigations showed that certain fibers of the posterior longitudinal band pass forward into the vesicoprostatic groove, and diverge slightly to form two muscular bands which pass downward on either side of the urethra, and, at its upper level, swing medially to form a loop about the urethra (external arcuate). The fibers from the circular layer of the detrusor pass around the bladder to a point just opposite the vesical neck; here some of the fibers from the region posterior to the vesical orifice swing downward and forward obliquely and pass as thin bands within the loop of the external longitudinal muscle, and, swinging around the urethra in the region opposite the verumontanum, form a loop about the urethra (internal arcuate).

The opening of the vesical orifice during micturition, according to these investigators, is not an inhibitory action but is primarily the result of the contraction of the powerful trigonal muscle which passes in the form of an arc through the weaker arcuate muscles at the vesical orifice and pulls them mechanically open on contraction. This view was confirmed by endoscopic and cystoscopic studies, as the trigonal muscle was seen

to contract and pull open the vesical orifice. Since pharmacological and embryological studies show that the trigonal muscle has an origin and nervous control different from those of the rest of the bladder, it is reasonable to suppose that it has independent powers of contraction and relaxation. The investigations of Wesson showed that the trigonal muscle is placed superficially in regard to the other muscles at the bladder neck, and that it passes downward and forward over the posterior border of the vesical orifice to form an internal longitudinal layer over the posterior aspect of the prostatic urethra, eventually reaching an insertion in the region of the verumontanum. The vesical and urethral sections of this muscular structure do not lie in a single plane, but are set at an angle which occurs at the vesical orifice, corresponding to the uvula vesicae. In contracting, the trigonal muscle straightens out this angle and draws back the lower lip of the vesical orifice, thus pulling open the internal sphincter. Young and Wesson found that removal of the trigone results in difficult and incomplete micturition; but that if one-half of the trigone is removed, the remaining half functions and the bladder can be entirely emptied. The same is true of a split trigone, although a split trigone is functionally inferior to one with its median bar intact.

While Young and Wesson have described the downward action of the trigonal muscle in straightening out the angle formed at the uvula vesicae, they have not stressed the importance of its peculiar triangular form. According to Macalpine, the two ureteral ridges (Bell's muscles) converge at the vesical orifice and, as they enter this opening, alter their course and run side by side down the urethra. When contracting, these two divergent limbs must become straightened out, and thus exert an outward as well as a downward traction on the orifice, in this way opening it transversely as well as vertically.

(McCrea's Theory.) McCrea's investigations led him to conclude that two systems of circular fibers go to form the internal "sphincter." Three muscular components form the basis of his description: (1) the detrusor ring, (2) the urethral loop with internal and external portions, to which he confusingly applies the terms "internal sphincter" and "external sphincter"; (3) the urethral bands.

The *detrusor ring* is a fibromuscular ring encircling the bladder neck, most marked anteriorly and laterally, and formed by fibers of the middle circular layer of the detrusor vesicae, certain tendinous fibers, and the terminations of most of the anterior fibers of the external longitudinal

layer of the detrusor vesicae. This fibromuscular mass appears to be anchored by the pubovesicalis muscle. Lateral expansions from this ring sweep downward and pass along the superficial and lateral aspects of the urethra. These fibers are best seen in the female; in the male the prostate interferes with their continuity. The detrusor ring contains numerous muscle bundles, which are plainly discernible anteriorly and laterally but are deficient posteriorly.

Immediately below this incomplete detrusor ring, the internal urethral orifice is surrounded by a sphincter composed of closely knit fibers which differ considerably in appearance from those of the circular coat, and it is improbable that this is a continuation of the circular layer of the detrusor vesicae. This sphincter lies below the crescent-shaped detrusor ring and is especially well marked posteriorly, where it extends for a short distance up into the trigonal region. Its fibers, especially the lower ones, extend downward as well as forward, and the lowest lie deep to the external loop. The muscle, viewed from the lateral aspect, therefore, appears fan-shaped. To this proximal and internal loop McCrae, like Henle, applies the term *internal vesical sphincter*.

The distal and external loop—*external vesical sphincter*—is formed from the posterior longitudinal unstriated muscle together with striated fibers derived from an upward prolongation of urethral fibers. Together with the proximal and internal loop—*internal vesical sphincter*—it forms a band which embraces the proximal urethra above the prostate, just distal to the internal urethral orifice. This is a very distinct ring in the infant, and is identical in both male and female.

A noteworthy point, of which McCrea found no previous record, is the presence of striated muscle fibers (voluntary) intermingling with the smooth muscle fibers in the trigonal region—a finding of considerable functional significance. He observes:

"Their course is very similar to that of the fibers in the internal sphincter; they pass downwards and forwards on each side from the trigonal region and lie between the posterior longitudinal fibers and the internal sphincter; they ultimately join the external sphincter. They extend an appreciable distance above the vesical orifice and their general form is that of a horseshoe. Their presence may help to explain the voluntary movement of the trigone, which Young has noted, and which may be observed during a cystoscopic examination if the patient be directed alternately to 'pass water' and to 'hold water.' . . . The whole picture of these muscles suggests that the trigonal region belongs to the urethra and has become incorporated in the bladder, this view is borne out by what we know in embryology. The sphincteric fibers found beneath the trigone, both striated and unstriated, therefore repre-

sent the distorted posterior urethral wall, and the bladder muscles proper have no share in the sphincteric mechanism except through the fibers of the posterior longitudinal bundle."

The internal "sphincter" receives sympathetic motor fibers through the hypogastric nerves from the thoracolumbar portion of the cord and parasympathetic inhibitory fibers through the pelvic nerves of the sacral portion of the cord.

Blood Supply of the Bladder. The control of hemorrhage is a major problem in any surgical intervention in and about the bladder, particularly the vesical neck. A thorough knowledge of the distribution of the vessels likely to be encountered when operating in this region is essential to the surgeon; yet there is a notable lack of text-book and other published material regarding this phase of vesical anatomy. The chief sources of information concerning the vascular supply of the bladder and vesical neck are the studies of Fenwick (1885), Keiffer (1898), Farabeuf (1905), and Tsaknis (1929). It is noticeable that every one of these authors speaks of the paucity of information upon this important subject.

The Arteries. The bladder receives its blood supply on each side from the superior vesical, inferior vesical, and anterior ascending vesical arteries, derived from the anterior trunk of the hypogastric (internal iliac) artery. When the arteries have reached the bladder, they subdivide into numerous branches. These form a plexus from which are given off many tiny arterioles which penetrate the bladder musculature and course through the mucosa, eventually forming another plexus in the submucosa. The obturator and inferior gluteal arteries also supply small branches to the bladder, and in the female additional branches are derived from the vaginal and uterine arteries.

The *superior vesical artery* arises from the umbilical artery, passes medially to the upper portion of the bladder, and anastomoses with the other vesical arteries.

The *inferior vesical artery* is a bifurcation of the genitovesical, the other branch being the prostatic artery. The course of these vessels roughly parallels that of the ureter of the corresponding side, and their entrance into the bladder is close to the point where the ureter pierces the bladder wall. Here the main artery on each side divides into several branches, a number of which take their course to the vesical neck while others are distributed to the base and the lower part of the lateral walls, and some to the antero-inferior and postero-superior walls. At the base of the

bladder the inferior vesical artery anastomoses with branches from the prostatic artery.

As the point of origin of the genitovesical artery is extremely variable, the surgeon is by no means certain of finding any or all of its branches where anatomical charts place them. The main trunk sometimes runs in front of the ureter, and again considerably behind it. The point of bifurcation likewise varies markedly in different individuals. In general, the origin of the genitovesical artery is high up if the artery is found to pass in front of the ureter. This origin depends, in turn, upon the relation of the ureter to the hypogastric artery. If this is abnormal, so that the hypogastric artery comes into relation with the ureter very high up, the genitovesical (which originates in the hypogastric) will be forced to descend behind the ureter. In apparently normal persons, therefore, there may be found a divergence all the way from one or two millimeters to a centimeter and a half intervening between the ureter and the genitovesical artery. The small branches reaching the vesical neck will be correspondingly altered in their positions.

At the point where the genitovesical artery bifurcates into the inferior vesical and the prostatic, the arterial branches are so enmeshed in vesical veins that it is often difficult to trace them without resorting to dissection. Arteries, veins, and nerves surround the urethral orifice and the upper third of the urethra, forming what Tsaknis terms the *urethrovascular pedicle*.

In general, therefore, it is the inferior vesical arteries (branches of the genitovesical) which supply the bladder neck and the trigonal region, anastomosing with offshoots of other vesicular arteries and the hemorrhoidal branches. Sometimes branches of the vesiculodeferential artery are directed toward the base of the bladder.

The Veins. The veins of the bladder drain anteriorly into the prostatic plexus (of Santorini) and into the lateral vesical plexus situated near the point where the ureter penetrates the bladder wall. They eventually empty into the hypogastric vein.

The vesical veins may be divided, for the convenience of description, into the anterior, lateral, and postero-inferior groups.

The *anterior veins* arise in the dome of the bladder and pass through the umbilical and prevesical fascia and the allantoid sheath in the general direction of the bladder neck, where they anastomose with the lateral veins. After passing between the two pubovesical ligaments, or, occasionally, behind them, these veins empty into the plexus of Santorini.

The median veins, which are larger than the rest of this group, can easily be injured during a suprapubic cystostomy, so that care should be taken to make the incision between them.

The number of *lateral veins* varies considerably in different individuals, but they are always numerous. Descending laterally through the allantoid sheath, they empty into either the vesical plexus or the plexus of Santorini. They also anastomose freely with the anterior and posterior groups.

The *postero-inferior* group includes the veins from the postero-superior wall and its peritoneal covering, the bladder neck, and the trigonal region. The veins of the postero-superior bladder wall are visible as soon as the peritoneum is exposed. They all take a downward course but frequently diverge as they descend so as to run off at acute angles. At each side they anastomose with the veins of the lateral and anterior groups. Most of them eventually reach the lower wall of the bladder and empty into the plexus of Santorini. The veins which arise at the trigone and vesical neck course through the posterior layer of the allantoid sheath, taking a forward and upward, then backward, course to empty into the plexus of Santorini in front and the vesical plexus behind.

A knowledge of these blood vessels and their relations is of the utmost importance to the surgeon. In addition, he should be prepared to deal with wide variations from what has more or less arbitrarily been accepted as normal.

The Lymphatics of the Bladder. The lymphatic vessels of the bladder originate in the mucosa whence they pass through the musculature to the external surface. Those from the anterior wall drain into the external iliac glands. In their course are situated two groups of minute nodes: an *anterior vesical*, in front of the bladder, and a *lateral vesical*, in relation to the lateral umbilical ligament. The vessels from the posterior surface and trigone drain into the hypogastric, sacral, and external and common iliac nodes. Those draining the postero-superior surface traverse the lateral vesical nodes.

Innervation of the Bladder. The innervation of the bladder is described under *Innervation of Micturition* (p. 969).

C. ANOMALIES OF THE BLADDER

The various congenital anomalies of the urinary bladder are the results of arrested or abnormal embryological development. Ordinarily, the small lumen of the urachus is practically obliterated at birth by

proliferated and desquamated epithelial cells from its lining membrane. Occasionally, however, there are deviations in the process of this degeneration, and the canal remains completely or partially patent, resulting in urinary fistulas, discharging umbilical sinuses, diverticula, and cysts. Failure of the fetus to develop an anterior wall results in exstrophy of the bladder. Other, rarer anomalies are absence of the bladder, double bladder, and hour-glass bladder. Congenital diverticula appear to be rare, although authorities differ regarding the etiology of vesical diverticulation, some claiming that all such diverticula are of congenital origin and others that they are acquired. Since obstruction appears to be a constant factor in diverticulum, whether congenital or acquired, and since no useful purpose is served by distinguishing between the two forms, they will be considered together (Diverticulum of the Bladder, p. 1080).

Absence of the Bladder

Absence of the urinary bladder is extremely rare, only a very few cases having been recorded. It is usually associated with other congenital abnormalities. The ureters open on the body wall or into the urethra.

Duplication of the Bladder

It is impossible to ascertain the true incidence of double bladder, since many cases of diverticulation were described as vesica duplex in the older literature. It is undoubtedly a very rare anomaly, however. Cathelin and Sempé (1903) collected 32 cases of double bladder from the literature, only 17 of which they considered authentic.

Etiology. Vesical duplication is due to an isolation of each half of the bladder in its fetal development. The normal single bladder, as described under Embryology, is the developmental end-product of the complete fusion of the vesical portion of the two mesonephric ducts. Incomplete coalescence, of various degrees, results in such anomalies as true double bladder, hour-glass bladder, and multiple loculations.

Pathology. In true double bladder the two separate halves, each with its ureter, usually unite at the base to empty through a common urethra. Nesbit and Bromme (1933) reported a case of duplication of the bladder, penis, and corpora cavernosa, in which two incomplete urethras opened into distinct right and left bladders with no communication between them. A single normal ureter entered each bladder. Neither bladder contained a trigone.

An apparent duplication may be produced by an intravesical membranous septum which may be placed sagittally, dividing the bladder into right and left compartments, or in the frontal plane, giving anterior and posterior chambers. The two halves usually communicate with each other by a small perforation, and in almost all cases each half is entered by a ureter.

Treatment. Any treatment would depend upon the pathological changes and symptoms produced by the abnormality. Most of these maldevelopments occur in association with some other congenital anomaly, and the majority of the reported cases were found at autopsy.

Hour-Glass Bladder

The term "hour-glass" has been loosely applied to various deformities of the bladder, including diverticulum, patent urachus, and certain acquired hypertrophic and cicatricial transverse ridges which develop in the presence of lower-tract obstruction or follow trauma or infection. True congenital hour-glass bladder is one in which the viscus is divided into an upper and a lower compartment, of varying relative size, by a partial transverse diaphragm. There is a narrow channel of communication between the two chambers (as in an hour-glass), which varies considerably in diameter. The ureters may enter the lower chamber of the bladder, as in the cases reported by Fothergill, Müller, Passow, Caulk, Kretschmer and Morris, Young, Kearns and Turkeltaub, and Eisenstaedt and McDougall; or they may enter the upper chamber, as reported by Detweiler, Fuller, Cutler, and others. The anomaly, although apparently very uncommon, is of great diagnostic importance when it does occur.

Etiology. A number of theories have been advanced to account for this anomaly. The most plausible would seem to be that either type of hour-glass bladder is the result of an unequal growth of the normally separate anlagen of the bladder. In support of this view Eisenstaedt and McDougall point out that the portion of the bladder between the ureteral orifices and the colliculus is of mesodermal origin, while the bladder cavity itself is of entodermal origin; that the anlage of the ureter is gradually taken up by the anlage of the bladder, and any failure of perfect coalescence of these two structures of different origin could produce transverse folds or fibromuscular ledges either above or below the entrance of the ureters into the bladder.

Pathology. The pathological changes in the bladder are largely the

result of interference with the normal functioning of the detrusor muscle due to the presence of the abnormal fibromuscular diaphragm. One chamber must empty into another, resulting in prolonged, difficult micturition, with, usually, incomplete emptying of the bladder. Residual urine ultimately develops, particularly if the communication between the two compartments is narrow, and the onset of infection produces the usual symptoms of cystitis. The increased effort necessarily put forth by the bladder musculature eventually causes hypertrophy of the wall.

Symptoms and Diagnosis. The symptoms are variable and in no way pathognomonic. In some of the reported cases there was a history of difficulty in emptying the bladder in childhood; but in other cases no symptoms were manifest until well past middle life, when the presence of the congenital ledge increased the severity of symptoms produced by unrelated factors, such as obstructive changes at the vesical neck.

The diagnosis is made by cystoscopy and cystography.

Differentiation must be made from patent urachus, which is usually easy, and from acquired transverse septums and diverticula. The last may be difficult. Important differential points are: (1) the history (diverticula usually developing subsequent to an obstruction); (2) consistent lack, in the diverticulum, of the muscular elements and their arrangement, as seen in the bladder; (3) the smoothness of the mucosa covering the thick, shelf-like division in the hour-glass conformation in contradistinction to the wrinkled mucous membrane invaginated into a diverticular cavity (Kearns and Turkeltaub).

Treatment. Eisenstaedt and McDougall recommend surgical resection of the constricting septum, which, in their case, was followed by a remarkable return to normal function and normal outline of the bladder. Caulk strongly advocates complete resection, which was easily accomplished in his own case (in which the ureters opened into the lower chamber), but would not, of course, be feasible when they enter the upper chamber. Other authors have recommended incision.

Exstrophy of the Bladder

Definition. Exstrophy of the bladder is a congenital anomaly in which the anterior wall of the bladder and the corresponding portion of the anterior abdominal wall are lacking, so that the inner surface of the posterior bladder wall, partially everted, protrudes on the abdomen. Sometimes it amounts to only a slight exposure of a section of the trigone,

but in most cases the cleft is far more extensive. A careful examination will demonstrate that what, at first sight, appears to be a split in the pubic region, is actually only a separation of the recti muscles, usually confined to the mons veneris but in some reported cases reaching as high as the xiphoid process.

The essential factor in the condition appears to be an error or arrest in the development of the anterior part of the allantois and the lower segment of the abdominal parietes. The symphysis is absent and the an-

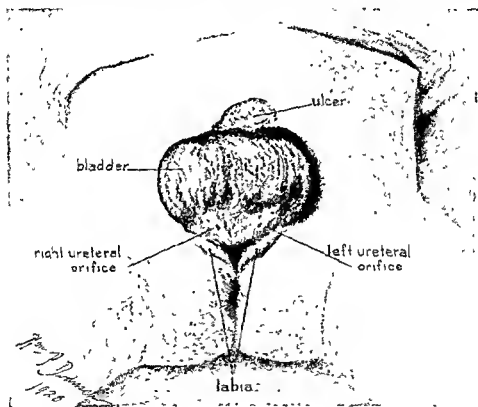


FIG. 221. Exstrophy of the bladder.

terior part of the pelvic girdle deficient because the pelvic bones are not normally developed. This results in a wide separation below of the recti muscles, so that they find their insertion in the pelvic bones by passing obliquely outward. This forms a space, roughly triangular in shape, into which the posterior wall of the bladder faces in the absence of the anterior wall. When exstrophy is complete, the symphysis will be separated for a distance of from 2 to 8 cm., the gap being filled in with connective tissue.

The ureters expel urine externally, and the constant dribbling of urine produces an intolerable condition. Epispadias is always present.

Incidence. The condition, fortunately, is relatively rare, although the literature upon the subject is extensive and the reported cases many. Reliable statistics place the incidence at about 1 case to 40,000 or 50,000 births. It is encountered more frequently in the male than in the female (5 to 1).

Etiology. There is still considerable disagreement about the etiology of exstrophy of the bladder and its accompanying anomalies. The various causative hypotheses fall into three groups: mechanical, pathological, and embryological.

(1) The mechanical theory: Exstrophy is the result of an intrauterine rupture of a completely formed bladder. The first stage in the process is the closing up of the urethra, causing retention of urine. The pubic bones, at this time scarcely cartilaginous and still ununited, are kept apart until they become hardened. At the same time the recti are separated, so that little by little, by the intravesical pressure of urine, the bladder presses against the abdominal wall and finally ruptures and forms adhesions to the borders of the split.

(2) The pathological theory, advanced by Keith and concurred in by von Geldern: Toxins from an endometritis, or any other form of infection or irritation, produce a separation of the lateral walls of the caudal portion of the embryo. Von Geldern explains this theory as follows: The arrest affects the parts which have not completed their embryonal development at the onset of the infection. When the development recommences, certain primitive embryonal structures are maintained and developed as such, and those that should have undergone differentiation, if no arrest had occurred, fail to do so.

(3) The embryological theories are quite numerous. Some authors consider the condition to be caused by failure of the primitive somatopleures to unite in the midline. Others, including Keibel, believe it may result from a persistent open blastopore. Still others attribute it to an arrested growth of the abdominal wall with extension of the cloacal membrane and cloaca, the splitting of which forms the anomaly. Gilis' theory is that normally the infra-abdominal wall is strengthened by the median growth of the protovertebral laminae of mesoderm, which give rise to the abdominal muscles and fasciae; but if these muscles are arrested in their development, so that they do not reinforce the cloacal membrane, the latter breaks down and exstrophy results.

Wyburn (1937), from a study of a series of embryos ranging from 1.4 to 40 mm. in length, concluded as follows regarding the etiology of exstrophy: (1) At an early stage the cloacal membrane is a relatively large area of contact of ectoderm and entoderm extending some distance along the allantoic diverticulum; (2) the allantoic cloacal membrane is later obliterated by the mesoderm pressing in toward the midventral line between the ectoderm and entoderm; (3) extroversion of the bladder is due to mesodermal deficiency, particularly of the processes of secondary mesoderm arising from the hind end of the primitive streak, following on which there is persistence of the primary extensive cloacal membrane, impaired development of the muscular coat of the bladder, of the symphysis pubis, and of the formation of the external genitals and the infra-umbilical portion of the anterior abdominal wall; (4) epispadias is a similar mesodermal error in a minor form.

Pathology. The various gradations of exstrophy have been classified as (1) *fissura vesicae inferior*, the form in which the symphysis is developed normally but the bladder is split inferiorly, (2) *fissura vesicae superior*, in which there is normal union of the pubis but a defect in the upper part of the bladder, and (3) typical complete exstrophy—by far the most common form. All three types offer problems of the greatest intricacy to the surgeon who undertakes their correction.

In typical complete exstrophy, there is absence of the symphysis pubis, with a varying degree of separation of the pubic bones. Between the separated fibers of the recti the bladder protrudes as a reddish fleshy mass above the level of the surrounding abdominal wall. The exposed mucosa is inflamed and sensitive. The ureteral orifices are plainly visible.

In the male, there is always epispadias and a short rudimentary penis, and frequently absence of the prostate and cryptorchidism, the scrotum being divided into two separate pouches by a deep furrow. In the female, the urethra appears as an open sulcus, the labia are merely indicated rudimentarily, and the clitoris is completely cleft, this cleft often continuing far within the genital canal, so that there is likely to be a bicornate uterus and, possibly, a double vagina. Other congenital abnormalities that are commonly associated are spina bifida, prolapse of the rectum, inguinal hernia, and atresia ani, with intestinal openings in the exstrophied bladder mucosa.

Vesical exstrophy is one of the most distressing anomalous physical conditions compatible with life. The entire surrounding surface is con-

tinually bathed in urine, so that there is constant local irritation and an ever-present urinous odor. Walking is always difficult, due to lack of the symphysis pubis, and the sufferers have a characteristic waddling gait. A child so afflicted is shunned by other children, so that the effect upon his character is very noticeable. He becomes timid, morose, and, in later years, often suicidal. About 50 per cent of these unfortunate persons die in infancy or early childhood from ascending infection and hydronephrosis, and relatively few of those not operated upon pass the twentieth year of life.

Occasionally carcinoma develops in the exstrophied bladder. Murphy, reporting such a case in 1924, was able to collect only 12 other cases from medical annals, and but few have been recorded since. This surprisingly low incidence, in view of the irritation and trauma to which the exposed bladder mucosa is constantly subjected, is probably partially accounted for by the fact that few of these patients live to the so-called "cancer age."

Diagnosis. The diagnosis is easily made upon local inspection.

Treatment. The treatment is wholly surgical, and is discussed under Surgery of the Bladder (p. 1122).

Congenital Hypertrophy of the Vesical Neck

Congenital contracture of the vesical neck, resulting from muscular hypertrophy, has been quite frequently described, especially by French authors. This condition produces the usual symptoms of urinary obstruction: frequency, small stream, hesitancy, difficult urination, pyuria. Cystoscopic examination reveals the changes at the vesical neck, as well as the typical changes of back pressure, such as trabeculation, cellules, diverticulation, and hypertrophy of the interureteral ridge.

Treatment. Occasionally a patient is cured by dilatations. Otherwise, treatment consists in resection of the hypertrophied tissue with the resectoscope.

Patent Urachus: Urachal Fistulas: Urachal Cysts

Etiology and Pathology. In the normal adult the urachus reaches only one-third of the distance from its point of attachment at the apex of the bladder to the umbilicus, and is attached to the posterior aspect of the navel by the fibrous remnants of the obliterated hypogastric arteries. Its epithelial canal is never completely obliterated by fibrous tissue, but retains a bore of about 1 mm. (Berg). Ordinarily, however, this small

channel is completely obstructed at birth by proliferated and shed epithelial cells and debris, which accounts for the rarity with which urine is found to pass upward from the bladder. The epithelial cells tend to proliferate outward into the dense connective tissue layer which surrounds and supports the lining membrane of the normal urachus.

In approximately two out of three persons the lumen of the urachus is separated from the bladder proper by a transverse mucous fold; but in the third instance this partition fails to develop, the lumen remains completely or partially patent, and what is known clinically as persistent or patent urachus results.

Acquired abnormalities are the results of urinary obstruction, either with or without some defect of development.

Various attempts have been made to classify the clinical conditions resulting from disturbances of obliteration of the urachus. The abnormalities to be recognized may be listed as follows:

(1) Complete patent urachus. The channel is open all the way, and forms a continuous communication between the bladder and the external surface at the navel.

(2) The urachus patent at the vesical end and closed at the umbilical end. This type may persist unrecognized throughout life, but when associated with obstruction of the lower urinary tract, may result in a diverticulum. Infection, with discharge into the bladder, will account for some cases of recalcitrant cystitis and pyuria. In the presence of lower-tract obstruction or increased intravesical pressure, urine escaping from the bladder into the open terminal urachal canal may extravasate to the umbilicus, to be discharged at the external surface, thus converting the externally blind canal into a complete patent urachus. These acquired patent canals are confused in the literature with congenital patent urachus.

(3) The urachus patent at the umbilical end and blind at the internal (vesical) end. In this form the desquamated epithelium and debris may stagnate and, if there is secondary infection, produce a mucoid or mucopurulent discharge from the navel. The skin about the discharging sinus is reddened and excoriated, and there may be a tender inflammatory mass. Large umbilical granulomas may develop.

(4) The urachus closed at both the vesical and umbilical ends, with the lumen patent only in the midportion. This type persists unrecognized throughout life unless a urachal cyst forms.

(5) Vesico-umbilical fistula. In this condition the bladder, which

normally descends at birth, is undescended or incompletely descended, and there is no urachus, the apex of the bladder lying at the umbilicus. In the presence of obstruction, there may be leakage of urine through the apex of the bladder at the umbilicus.

(6) Urachal cysts. These are uncommon. Cross (1935) found reports of only 96 cases. They may form at any point between the apex of the bladder and the umbilicus if a small portion of the duct remains patent. The majority (over 50 per cent) are found at the vesical end of the urachus, the portion of the tract most commonly patent. They vary greatly in size but may reach enormous dimensions. Patel and Labry (1926) collected from the literature 10 cases of large urachal cysts and added one of their own. The cyst may contain urine, a mucoid fluid from the cyst wall, a serous transudate, pus, blood, cholesterol, fat cells, epithelium, or fibrin (Bauer, 1931). The urachal cyst has no tendency to resorption. Spontaneous rupture, which is uncommon, usually occurs at the umbilicus, but may be into the peritoneal cavity. Infection of urachal cysts is frequent, and is evidenced by a painful, tender mass in the midline between the bladder and the umbilicus, abdominal pain, fever, and gastrointestinal disturbances. An infected urachal cyst may empty suddenly into the bladder, producing an acute cystitis, the underlying cause of which may readily be overlooked. Differentiation between a urachal cyst communicating with the bladder and a true diverticulum may be extremely difficult. The chief symptoms of large cysts are those of tumorous compression, with severe abdominal pain, and intravesical hemorrhage.

Incidence of Urachal Anomalies. Congenital patent urachus, with discharge of urine at the umbilicus, is rare (87 cases up to 1932, Ducleaux and Blondin). It is preponderant in the male in the approximate ratio of 2 to 1. At the Children's and Infants' Hospital, in Boston, in a total of over 200,000 admissions, the diagnosis of congenital patent urachus, with discharge of urine at the umbilicus, has been made 3 times; and among 15,000 admissions to the Brady Urological Institute (Baltimore) there were only 3 presenting a patent urachus (Mahoney and Ennis, 1936). Herbst (1937) found an approximate total of 150 reported cases of both congenital and acquired patent urachus, dating back to 1550, when Bartholomaeus Cabrolus, in his *Alphabet Anatomique*, reported a case in a woman of 18 years, "on whom he performed an operation for the re-establishment of the normal channel of flow of urine, the procedure consisting in ligation of the umbilical protrusion and dilatation of the

urethra." Herbst estimated the **apparent ratio** between the congenital and acquired forms to be roughly as 5 to 4. There were 108 cases in males and 44 in females.

Diagnosis of Urachal Anomalies. The diagnosis and early treatment of a patent urachus are important, in view of the frequency of a subsequent infection, neoplastic change, or calcification of the urachal contents. Congenital complete patent urachus is usually discovered at birth, but in the absence of a profuse urinary discharge may easily be overlooked because of its rarity. The urachal fistula which occurs later in life is probably attributable to a persistent urachus of congenital origin which was overlooked during the postpartum period. The blind type may easily go unrecognized until infection sets in, or the secretory activity of the lining membrane produces a urachal cyst, or it is converted into a complete patent urachus in consequence of rupture of the closed end.

In a patent urachus the sinus runs downward in the midline. The discharge, which may be profuse or may amount to only a few drops, has the characteristics of urine. Cystography is useful in demonstrating the tract.

If infection is present in a complete patent urachus, or in one that is patent at the umbilical end, the chief complaint is of an intermittent, thin, watery secretion from the umbilicus, which periodically becomes purulent and is then associated with redness and tenderness about the umbilicus or with an umbilical tumor. Infection in a urachus patent only at the vesical end is likely to be mistaken for a cystitis.

Treatment. Urinary fistulas are best treated by complete extra-peritoneal excision of the tract, with closure of the bladder wall by sutures. This should be done as early as possible because of the danger of such tracts becoming infected. A sinus which is blind at the vesical end often may be closed by electrical cauterization; or it may be completely excised, great care being taken not to injure the peritoneum.

Uninfected urachal cysts can ordinarily be excised extraperitoneally without difficulty. In the massive cysts, however, there are usually extensive peritoneal adhesions, and in these cases the cyst should be extirpated with the adherent peritoneum. Puncture is contraindicated, as the fluid reforms rapidly.

Abscess-formation, resulting from the infection of a urachal cyst, requires preliminary drainage as a rule, followed by radical excision at a later date.

It should be emphasized that when a patent urachus is encountered in early life diligent search should be made for an obstruction of the lower urinary tract (phimosis, congenital valves of the posterior urethra, congenital stricture of the meatus) which may be the underlying cause of the patent urachus. The removal of such an obstruction, if present, will usually result in prompt closure of the fistula. If no obstruction is found, or if the fistula fails to close, operation upon the fistula is indicated.

D. PHYSIOLOGY OF THE BLADDER

In man, the important function of the urinary bladder is the storage and the evacuation of urine.

The urinary bladder in man normally acts as a receptacle for urine for short periods. In some lower forms of animals, however, the bladder may also function as a reservoir for the accumulation of a water reserve which is reabsorbed by the animal in time of drought. It is a well-known act that turtles reabsorb the fluid from the bladder in dry periods.

It has been definitely proved that absorption is much more active from the posterior urethra than from the bladder, but there is no question that certain substances—sugar, urea, alcohol, sodium chloride, cocaine, nicotine, pilocarpin, strychnine, alypin—can be absorbed by normal, and, to an even greater extent, by abnormal vesical mucosa.

Micturition

Micturition—the voiding of the urine—is a complex combination of reflexes involving the bladder, its sphincters, the trigonal muscle, and the accessory urethral and perineal muscles. A knowledge of the musculature and innervation of micturition is necessary in order to understand the complicated mechanism of bladder emptying.

The Musculature of Micturition. Five groups of muscles are concerned in the act of micturition: (1) the detrusor vesicae, (2) the internal “sphincter” (composed of the detrusor ring, urethral loops, and urethral bands), (3) the trigonal muscle, (4) the external sphincter, (5) the accessory urethral and perineal muscles. The first three have been described under *Musculature of the Bladder* (p. 950).

The External Sphincter. The external sphincter (sphincter urethrae) is formed of striated muscle fibers, and is under voluntary control. In the male, it is composed of prostatic, urethral, and urogenital fibers. The fibers of the upper or prostatic portion have their origin in the lateral surface of the prostate near the vesical orifice, where they lie in close

relationship to the fibers of the external urethral loop. (This portion is sometimes called the *sphincter externus vesicae*.) As they pass downward the fibers increase in numbers but extend only about half-way round the urethra until the apex of the prostate is reached; from here on they surround the urethra to meet posteriorly in a raphe. Below the apex of the prostate the fibers of the external sphincter lie between the two layers of the triangular ligament. The external sphincter does not make a complete circle of the urethra, but ends in a raphe of connective tissue behind the membranous urethra. Because the prostatic tubules invade the inner circular layer of the posterior urethra, Wesson believes that its value as a sphincter muscle is considerably diminished.

The fibers of the external sphincter have sensory innervation and are under control of the will. The innervation is derived from the sacral portion of the cord, being carried by the somatic fibers of the pudic nerves.

The Accessory Urethral and Perineal Muscles. Certain accessory urethral and perineal muscles—(1) the bulbocavernosus muscle and (2) the prostatic fibers of the levator ani with the recto-urethralis muscle and the urogenital diaphragm—also have a part in expelling the urine (and semen) and giving continence. The bulbocavernosus arises from the central point of the perineum and passes upward and forward, completely surrounding the bulb of the urethra. These accessory muscles are held in a delicate balance of tonicity which prevents incontinence. They also exercise a peristaltic action with the urethral band, thus not only emptying the bladder but stripping the urethra at the end of urination (and ejaculation) so that there is no dribbling.

The Musculature of Micturition in the Female. Sexual variation in the musculature of micturition is relatively insignificant and is due mainly to interposition of the prostate gland. The external sphincter in the female extends fibers around the vagina, and, in the absence of the prostate, extends farther up the urethra. It forms a complete circle about the urethra only in its lower half; farther up the fibers merely make a semicircle and terminate in the lateral wall of the vagina. The urethral bands in the female are definite lateral extensions, partly of urethral and partly of vesical origin. In the male these bands merge with the prostate. Otherwise, the musculature of the female resembles the arrangement of the male, with similar innervation and mechanism.

The Innervation of Micturition. The innervation of the bladder and the part played by various groups of nerves in the control of urination

have occupied the attention of many eminent physiologists, neurologists, and urologists. Experimental investigation in animals and pathologico-clinical investigations in man have gradually added to knowledge of the structure and function of the nerves supplying the bladder and posterior urethra, but the subject is complex and as yet not fully understood. Our knowledge of the neurophysiology of the bladder is based largely on animal experimentation. But as lack of uniformity is a notorious feature in the innervation and anatomy of the bladder in different animals, deductions drawn from a single type cannot be universally applied. Undoubtedly, errors and confusion have arisen from a too close application to man of the findings in animals.

The literature on the nervous control of the bladder is vast. The masterly review of Fearnside covers the ground up to 1917 and the monograph of Dennig reviews the subject up to 1926. Since then important observations made on man have been reported by Learmonth, Langworthy and his collaborators, Ortmann and Christiansen, Denny-Brown and Robertson, and others.

The Nerve Pathways to the Bladder. There are three nerve pathways to the bladder and the associated muscular structure concerned in micturition: (1) the *hypogastric*, originating in the thoracolumbar portion of the cord; (2) the *pelvic*, originating from the sacral plexus; (3) the *pudic*, also arising from the sacral plexus. All three contain both efferent and afferent fibers. The various reflexes on which the process of micturition depends are set into action through these pathways.

(1) **THE HYPOGASTRIC PATHWAY (SYMPATHETIC).** The hypogastric, or presacral, nerves are derived from the lowest thoracic and upper lumbar nerve-roots, and send their fibers by way of the white rami communicantes and the lumbar or inferior splanchnic nerves to the lumbar portion of the collateral sympathetic chain of ganglia which lies in intimate relations with the abdominal aorta and its branches. They then join the inferior mesenteric ganglia along the line of the gray rami. Most of the fibers form synapses at the inferior mesenteric ganglia, and their continuations beyond these ganglia eventually are united with the ganglia in the lower part of the abdominal sympathetic trunk. A few fibers from the aortic plexus have their synapses in the vesical wall, which they reach from these same lower ganglia of the abdominal sympathetic trunk.

The function of the hypogastric nerve fibers supplying the bladder has been a subject of wide research and considerable controversy. They

are regarded by most investigators, however, as being motor to the internal sphincter, trigone, and the smooth muscle of the proximal part of the urethra, and inhibitory to the detrusor vesicae. They also cause contraction of the ureteral orifices and of the muscles of the seminal vesicles, ejaculatory ducts, and prostate. Stimulation of the hypogastric nerves gives rise to contraction of the internal sphincter. The ability of the sphincter to remain closed after section of these nerves proves, however, that it must also possess an inherent tonus of its own. "We are forced to conclude," says Learmonth, "that maintenance of closure of the internal sphincter depends upon its inherent tonus, which in turn depends upon the integrity of reflex fibers in the parasympathetic pathway; and that its sympathetic supply merely reinforces this closure."

McCrea and Macdonald (1934), after extensive experimentation upon cats, decided that the hypogastric nerves may produce either motor or inhibitory effects on the detrusor, and question whether they have any influence at all on the internal sphincter. Section of the hypogastric nerves, they found, does not cause relaxation of the sphincter either in the cat or in man; and following presacral sympathectomy, micturition appears to be absolutely normal apart from occasional instances of slightly increased frequency. These investigators believe, therefore, that the hypogastric nerves, although functioning in bladder control, may be dispensed with without marked alteration in function and are not essential to a satisfactorily acting bladder.

Denny-Brown and Robertson (1933), from studies of the bladder in spinal lesions in man, conclude that the hypogastric nerves do not take part in the mechanism of micturition, but that they serve as an inconstant pathway for the pain of powerful vesical contraction, though not for the sensation of normal desire to micturate.

Clearly, the precise action of the hypogastric nerves on the internal sphincter and musculature of the bladder wall is still to be determined, and further observation in man is needed before any definite conclusions can be drawn as to their importance in bladder function.

The innervation of the trigonum musculature appears to be exclusively sympathetic, while in the rest of the fundus it is both sympathetic and parasympathetic. Macht, working with Young and Wesson, in pharmacological studies upon specimens of human trigonal muscle and tissue from the fundus, found that the trigonal muscle contracted in response to epinephrin and ergotoxine, indicating that the trigone is innervated by true sympathetic nerve-endings, but failed to contract or relax in

response to pilocarpin, physostigmin, and atropine, indicating that it is devoid of parasympathetic nerve-endings. The fundus gave reactions for both sympathetic and parasympathetic nerves. Experiments upon the trigonal muscle with nicotine gave a response pointing to the presence of ganglionic structures in that layer. That the sympathetic system controls the trigonal region as well as the internal sphincter in man is also the conclusion of Learmonth.

(2) THE PELVIC PATHWAY (PARASYMPATHETIC). The pelvic nerves (*nervi erigentes*) are the nerves principally concerned with urination. They arise from the anterior primary divisions of the second and third or third and fourth sacral nerves. They do not pass into well-defined ganglia, but form the vesical portion of the hypogastric plexus, which spreads over the bladder wall and supplies the unstriated muscle of the bladder, the urethra, and corpora cavernosa.

The pelvic nerves are motor to the detrusor vesicae and inhibitory to the internal sphincter. The sympathetic and parasympathetic nerves are therefore reciprocal in their actions.

Both the hypogastric and the pelvic nerves transmit sensory impulses, but the pelvic nerves (parasympathetic) carry the larger part of the afferent fibers of the bladder. By the parasympathetic pathway also travel at least a part of the sensory nerves of the posterior urethra.

Learmonth has summarized the afferent activities of the sympathetic and parasympathetic pathways in man as follows: *Pain* impulses reach the central nervous system by way of both the sympathetic and parasympathetic systems, but principally via the latter. Impressions of *distention of the bladder* are also conveyed via both systems. Afferent fibers transmitting *tactile* and *thermal* sensibility appear to be present and to traverse the parasympathetic system only. Most, if not all, of the afferent fibers which subserve the *micturition reflex* reach the central nervous system by the parasympathetic system. The sympathetic pathway from the bladder, concludes this observer, is not essential for the act of micturition.

(3) THE PUDIC PATHWAY (SOMATIC). The pudic nerves derive from the third and fourth segments of the sacral portion of the cord. They are motor to the external sphincter and the accessory urethral and perineal muscles and are sensory to the posterior urethra. These somatic fibers do not pass through the hypogastric ganglia.

Barrington found that the integrity of the pudics is necessary both for urethral tone and its relaxation when the contents of the bladder are

artificially expressed; also, that only when the pudics remain intact can the experimental animal be conscious that it should evacuate the bladder. Learmonth, on the other hand, claims that the sensation of the posterior urethra depends on fibers reaching it along autonomic routes; that, as has repeatedly been shown, following bilateral pudic neurectomy, the act of passing urine can be carried out in a normal manner; and that from the physiological standpoint it may be concluded that only the parasympathetic pathway (afferent) is essential to the act of micturition.

To summarize: The involuntary musculature of the bladder wall and of the internal sphincter receives innervation from (1) the thoracolumbar sympathetic pathway via the inferior mesenteric ganglion and the hypogastric nerves and (2) the sacral plexus by way of the pelvic (parasympathetic) nerves. These two pathways intermingle in the vesical plexus of outlying ganglion cells and fibers which directly innervate the bladder and sphincter. Animal experimentation provides ample evidence of a direct reciprocal innervation of the detrusor and internal sphincter. The voluntary external sphincter and the associated voluntary perineal musculature are innervated by the pudic nerves (somatic), also derived from the sacral portion of the cord.

Peripheral stimulation of the cut pelvic nerves in animals causes contraction of the detrusor muscle with relaxation of the internal sphincter. Excitation of the hypogastric nerves induces contraction of the internal sphincter in all animals and in man (Learmonth), with or without inhibition of the detrusor according to the species of experimental animal (Elliott). Stimulation of the peripheral ends of the divided pudic nerves produces contraction of the external sphincter.

Stations and Tracts in the Central Nervous System Governing Micturition. Centers regulating micturition are situated in the mid-brain, hind-brain, and spinal cord. Bechterew and Mislawski, Frankl-Hochwart and Fröhlich, and Sherrington, in animals, found a cortical center which, on stimulation, caused changes in the musculature of the bladder. Czyblarz and Marbury described a cortical bladder center in man which lies in the Rolandic motor area.

The nervous control of the bladder has been extensively studied by O. R. Langworthy and a number of collaborators. Normal micturition, they found, is dependent upon a well-sustained contraction of the smooth musculature of the bladder wall. Lesion of the nervous system below the mid-brain results in disarrangement or incompleteness of this contraction. Transection of the brain-stem of the experimental animal (cat)

below the acoustic colliculi resulted in abolishment of the reflex causing contraction, followed by retention with overflow. This led them to conclude that tone in the bladder musculature is controlled by similar mechanisms to those that control tone in the striated musculature, and that this tonic mechanism is largely a function of the cerebral motor cortex and is effective at the level of the spinal cord. The tonic control is carried out from areas in the cephalic portion of the hind-brain.

Barrington's experiments with cats showed that destruction of a small portion of the hind-brain lying ventral to the internal edge of the superior cerebellar peduncle, and extending from the level of the motor nucleus of the fifth nerve behind to the anterior end of the hind-brain in front, abolished the animal's ability to micturate. Destruction of an area in the mid-brain extending from the ventral part of the posterior end of the cerebral aqueduct to just beyond the mesencephalic root of the fifth nerve caused permanent loss of the desire to micturate, although the reflex performance of the act was not impaired.

There is, as we have seen, a thoracolumbar center and a sacral center in the spinal cord. In addition, there are numerous peripheral ganglionic centers.

Pathologicoclinical investigations in man suggest that the descending and ascending paths of cerebrovesical impulses lie in the posterior portion of the lateral columns of the spinal column near the pyramidal tract.

Effects of Nerve Sections upon Micturition. Intact pelvic nerves are the most essential to the performance of normal voluntary micturition since they carry the chief motor and sensory fibers. Section of the hypogastric nerves alone results in either no change or but a slight frequency of micturition. Section of the pudic nerves alone leads to occasional slight incontinence but does not otherwise disturb the normal outflow of urine. Bilateral section of the pelvic nerve causes a profound depression of micturition with an atonic distended bladder (Elliott; Barrington). This condition changes in a few days to intermittent micturition in small jets, each expressed only by powerful effort in the cat (Barrington). Section of all three sources of innervation is followed after a brief period of retention by periodic discharge or automatic micturition (Dennig; Elliott; Wlasow, Denny-Brown and Robertson).

The Physiology of Micturition. The physiology of micturition has been carefully studied by physiological experimentation and, clinically, by endoscopy and cystoscopy, cystography, and cystometry, so that the normal process of bladder emptying is fairly well understood. Many

observers feel, however, that we have not yet solved the problem. There is considerable variation of opinion as to the sequence of events in normal human micturition, as well as the extent to which the bladder and sphincters, which possess a definite degree of autonomy, are subject to the control of the will.

The act of micturition, though essentially reflex in nature, is usually initiated by an effort of the will. It is only in the infant, and in certain pathological states, that micturition is a purely reflex act. Ordinarily, by the third year the normal child is able voluntarily to initiate and restrain the evacuation of urine. In the adult, micturition is voluntary either after the reflex desire has arisen, or before the desire has manifested itself and at will. In the latter form the act is started by a willed effort which apparently affects the lower centers in the same way as do afferent impulses arising from the full bladder or in other sensory reflexes.

The detrusor muscle exhibits both a sustained contraction (tonus) and intermittent contractions

The micturition reflex is largely dependent on the tension exerted upon the vesical contents. Mosso and Pellacani (1882) showed by experiments upon dogs and human beings that under one and the same pressure, observations upon the vesical contents at short intervals showed different volumes. They concluded that in a normal man the desire for micturition is stimulated when the pressure rises above 18 cm. of water, and pointed out that the stimulus exciting desire to micturate is closely related to intravesical pressure but is not directly related to volume. They also observed that the viscus responded to an increment in volume by an active diastole proportional to the volume of increment, and to a diminution in volume by an active systole similarly proportioned.

Subsequent workers have repeatedly confirmed this ability of the bladder to adjust its tone and thus adapt its capacity to changes in the volume of its contents, so that intravesical pressure is maintained at a constant level as volume increases over a moderate range. Denny-Brown and Robertson did not find a pressure of 18 cm. of water necessary to evoke desire for micturition—discomfort being sometimes extreme at much lower pressures. Resting vesical tension at moderate volumes varied from 5 to 10 cm. of water, they found; and this range they regard as the normal pressure of the vesical contents.

Tension is the stimulus for the sensory end-organs in the bladder wall. As urine enters the vesical cavity, coming intermittently by spurts from either ureter, the bladder wall responds to the increment in volume by

elongations of its muscle fibers, this being the response to stimulation of the "filling nerves" (hypogastrics). During this involuntary filling stage the internal sphincter is contracted in normal tonus.

The mechanism of bladder closure is imperfectly understood, but appears to involve the following elements: (1) tonic contraction of the internal sphincter; (2) involuntary relaxation of the detrusor vesicae; (3) hypothetical voluntary contraction of the internal sphincter; (4) voluntary contraction of the external sphincter; (5) voluntary contraction of the accessory urethral and perineal muscles. We know that following surgical or traumatic destruction of the external sphincter, the internal sphincter functions at will, and during seminal ejaculation with a full bladder, when the external sphincter is relaxed, the internal sphincter functions voluntarily, closing off the bladder. These facts point to a not wholly involuntary mechanism of the internal sphincter. As the bladder fills, this mechanical closure becomes increasingly effective. When filling invades consciousness, and is translated into the desire to void, voluntary closure is effected through reflex stimulation of the external sphincter and tonic contraction of the perineal musculature.

Voiding of the bladder contents depends on a complicated combination of reflexes. The chief factor in discharge is contraction of the detrusor in response to distention of the bladder, with an accompanying secondary relaxation of both sphincters. This reactionary contraction evoked by distention of the bladder is controlled by a restraining effect which at low volumes is subconscious in operation but intrudes upon consciousness in greater degree as volume increases (Denny-Brown and Robertson). A sensory impulse, derived from a given amount of distention of the bladder wall, reaches the sacral plexus by way of the pelvic (parasympathetic) nerves, is transmitted in the cord to the motor neurone of this reflex arc, and reaches the detrusor muscle and the musculature of the internal sphincter simultaneously, as a motor impulse, producing contraction of the detrusor and a reciprocal relaxation of the sphincter. The latter, in turn, sets up reflex impulses which result in relaxation of the external sphincter, and thus the bladder empties. The storage and discharge of urine take place, therefore, in a reservoir the distention of which excites a tendency to an automatic evacuation.

Micturition usually occurs, unless restrained, after from 250 to 300 cc. of urine have accumulated.

If, however, the time and circumstances are not such as to permit evacuation of the bladder, the vesical contractions responsible for the

discharge of the urine may be inhibited by voluntary effort, so that the bladder will once more be relaxed and the internal sphincter tightened. This is what is known as a "conditioned reflex," which is often cited as an example of the way in which nature bows to the demands and customs of civilized society. As a result, relatively great degrees of vesical distention may be reached before the reflex contraction of the detrusor results in emptying. "Voluntary restraint of micturition," observe Denny-Brown and Robertson, "has a direct effect on the contraction of the bladder, so that the spontaneous nervous discharges responsible for vesical contractions can be completely inhibited with ease. It is suggested that the site of impact of this inhibition is on outgoing neurons of the spinal cord. Contraction of the perineal musculature is closely associated with voluntary restraint, as is also direct and immediate closure of the external sphincter."

In voluntary micturition the following takes place: (1) The internal sphincter and prostatic urethra are voluntarily depressed by contraction of the levator prostatae and recto-urethralis, straightening the curve of the posterior urethra; (2) the bladder neck is opened (a) by relaxation of the tonic contraction of the internal and external sphincters, and (b) by the contraction of the trigonal muscle (Wesson, Young and Macht) and the pubovesical muscle (Heiss; McCrea)—the opposite pulls of these two muscles straightening the angle at the internal sphincter; (3) the detrusor vesicae contracts simultaneously with the trigone and with relaxation of the tonic contraction of the sphincters, and pressure is exerted by the voluntary contraction of the abdominal, respiratory, and rectal muscles; (4) the last drops of urine are expelled from the urethra by action of the bulbocavernosus muscle, preventing dribbling.

Though the abdominal muscles play a non-essential role in micturition, the act is usually started by the contraction of these muscles, and the flow of urine is also accelerated during micturition by their voluntary contraction.

Regarding the mechanism of the opening of the internal sphincter, two hypotheses have been advanced: (1) that it is opened mechanically by the pull of extensions of the trigonal muscle which pass within the grasp of the sphincter to insertions in the posterior urethra (Wesson, Young and Macht); (2) that its natural tonus is directly relaxed by inhibitory influences passing over the parasympathetic nerves, and that it is possible to accomplish this inhibition by the exercise of the will (Reh-fisch; Learmonth). Learmonth observed contraction of both the trigone

and the internal sphincter on stimulation of the sympathetic pathway, but contraction of the trigone was not observed to open the sphincter. It is probable that both processes—traction and active relaxation—play a part in the opening of the sphincter.

Measurement of Bladder Pressure (Cystometry)

Cystometry is the clinical study of the physiology of the bladder musculature (detrusor vesicae) by the simultaneous measurement of the intravesical pressure and the total fluid content of the bladder. This measurement is accomplished by means of a cystometer, and is the most exact method thus far devised of estimating the functional ability of the detrusor. As fluid is run into the bladder, the changing intravesical pressures are registered and plotted against the total volume of fluid in the bladder. The fluid may be introduced in a constant inflow or, as is usual in clinical practice, in a succession of equal amounts, each increment of fluid being followed by a reading. There is thus obtained a pressure curve which represents the response of the detrusor mechanism to gradual stretching and indicates its strength and resiliency. In addition, the patient's sensory reactions to the filling are registered and correlated with this pressure curve. These sensations include factors such as the first desire to void, the sense of bladder fullness, the point of filling at which pain is produced, etc. Cystometry is, therefore, a combined sensory and motor examination. The reading is most easily interpreted when plotted in the form of a graph.

Types of Cystometers. Various types of cystometers have been developed. That devised by Rose—to whom we are indebted for this "new diagnostic principle" as he rightfully termed it—utilized a continuous inflow, a manometer system, and tracings upon a revolving drum. Muschat and Johnson, in 1932, introduced a simplified apparatus in which the readings are taken by the interrupted method, and employing a mercury manometer. Simons' microcystometer (1937) has an accessory sphincterometer, which gives additional information relative to the status of the sphincters. Modifications and improvements from a wide range of viewpoints (Munro, Weyrauth, MacKenzie and Beck, Lewis and Langworthy, Lowsley and Hunt, Fig. 1) have made the cystometer more easily available to the practicing urologist, but in no way detract from the brilliancy of Rose's original achievement.

Uses of Cystometry: Interpretation of Cystometrograms. The complex mechanism of micturition is chiefly concerned with (1) the internal

and external sphincters, which retain the urine within the bladder until such time as it may be conveniently evacuated; (2) the trigonal muscle, the contractions of which pull open the internal sphincter; and (3) the detrusor vesicae, which, after having reached a certain degree of stretching, contracts and expels the bladder contents. Disturbance of the function of any one of these will upset the normal rhythm of urinary evacuation. Relaxation of the sphincters results in a greater or less degree of incontinence; loss of tone of the trigonal muscle causes partial or complete retention of urine, depending upon the amount of damage to the muscle; weakness of the detrusor also causes partial or complete retention. The urologist faced with any of these vesical derangements must resort to various means to determine the exact nature of the lesion responsible for the disturbance.

The state of the sphincters and the trigone can best be determined by cystoscopy, which permits one to note that the sphincters are relaxed or fail to close completely, or, in the case of the trigone, that there is only a very slight elevation of the floor of the bladder when the patient attempts to urinate. Cystograms are also of value in demonstrating a relaxed condition of the internal sphincter. Weakness of the detrusor cannot be determined accurately by the cystoscope. Characteristic, rather fine trabeculations may or may not be present, or, if present, may be unconvincing, so that personal judgment, based upon considerable experience, must be exercised. The cystometer, however, does afford a true gauge of detrusor function, and is our most valuable adjunct in the diagnosis of neurogenic disturbances of the bladder.

In diagnosing a neurogenic bladder one must interpret not only the pressure curve but its correlation with the sensory factors. The range of variations of the pressure curve in the normal is rather wide, and depends upon the general tone of the autonomic nervous system of the individual. Thus we find curves that are high normal and those that are low normal. Interpretation of the pressure curve alone may lead to errors of diagnosis. The range of variations of the sensory factors in the normal individual is, however, small. The first desire to void, in particular, is remarkably constant. The points of filling at which these sensations occur is, therefore, of great importance in indicating deviations from the normal, and must be correlated with the pressure curve.

In a normal bladder, there is a gradually rising curve, the first desire to void is around 150 cc. with a pressure in the bladder of 7 to 10 mm., the sensation of fulness is at about 250 cc., and the maximum voluntary

pressure 60 to 80 mm. In a myogenic bladder, the desire to void will occur around 150 cc. In the neurogenic bladder, the first desire to void occurs under 150 cc.; in the hypertonic bladder, the curve is high, and the maximal volume pressure over 80 mm.; in the hypotonic bladder, the desire to void occurs over 250 cc., the curve is flat, and the volume pressure under 60 mm.

When used in conjunction with cystoscopic and physical studies, cystometry finds its chief application in the differentiation of bladder dysfunctions caused by mechanical obstruction from those due to disturbances of innervation. The pressure curve of a bladder whose outlet is blocked by a hypertrophied prostate or other mechanical obstruction, will still be within normal limits. When dysuria is caused by a nerve lesion, however, the flat curve characteristic of such lesions is obtained. The response of a hypotonic detrusor to bladder filling has been described by Muschat as: *Flat curve, shifting of first desire to void to the right, and low voluntary pressure.* In many cases of chronic urinary retention caused by obstruction at the vesical neck, a thinning out of the detrusor musculature will be observable on cystoscopic examination. When the innervation of the bladder has been disturbed by a cord lesion or other factor, we may likewise see a thinned-out bladder wall. The cystoscope will not permit of differentiation, but with the aid of the cystometer this is easily accomplished. Cystometry has thus made a very important contribution to differential diagnosis by permitting us readily to distinguish between vesical irregularities of mechanical and neurogenic origin. Since operation is usually indicated in mechanical obstructions, but not in lesions of the nerves controlling the bladder muscles, unnecessary surgery can by this means frequently be avoided.

Cystometry has also been found useful in differentiating the various types of neurogenic bladders; in the study of cases in which neurogenic and obstructive factors are present in the same patient; for diagnosing certain diseases and injuries of the brain and spinal cord; as a means of noting improvement or regression of patients under active treatment; and in pharmacological and dynamic studies of the bladder.

Cystometry has contributed much to a better understanding of the urological symptoms of incontinence and retention—preoperative and postoperative. In the anuria following operations, particularly upon the prostate, it is often of great prognostic importance to be able to determine whether or not a neurogenic factor is operating. If the cystometer gives a curve practically or entirely within normal limits, the prog-

nosis is good. If the curve is flat, indicating hypotonicity, the outlook for a return to normal is distinctly poor. The cystometrogram also often aids in formulating a prognosis in urological procedures such as presacral neurectomy and plastic operations on the sphincters. Since cystometry may easily be carried out whenever catheterization is possible, and advisable, it will be found useful in many cases in which cystoscopy is, for one reason or another, contraindicated.

BIBLIOGRAPHY

- ABUREL, E., CHAUCHARD, A., AND CHAUCHARD, B.: Recherches physiologique sur l'innervation motrice de la vessie. *Compt. rend. Soc. de biol.*, 107: 1036, 1931.
- ARAÚJO, A. EIRAS DE: Fistula vesico-umbelical por persistencia do uraco. *Rev. Urol. de Sao Paulo*, 4: 197, 1937.
- AREY, L. B.: *Developmental anatomy*. Phila., W. B. Saunders Co., 1924.
- BARRINGTON, F. J. F.: The nervous mechanism of micturition. *Quart. J. Exper. Physiol.*, 8: 33, 1914.
- BARRINGTON, F. J. F.: The relation of the hind-brain to micturition. *Brain*, 44: 23, 1921.
- BARRINGTON, F. J. F.: The central nervous control of micturition. *Brain*, 51: 209, 1928.
- BARRINGTON, F. J. F.: The component reflexes of micturition in the cat. *Brain*, 54: 177, 1931.
- BARRINGTON, F. J. F.: The localization of the paths subserving micturition in the spinal cord of the cat. *Brain*, 56: 126, 1933.
- BAUER, C.: Klinische bedutung und histologischer bau der urachuszysten. *Ztschr. f. Urol.*, 25: 807, 1931.
- BECHTEREW, W. AND MISLAWSKI, N.: Ueber centrale und periphere darminnervation. *Pflüger's Arch. f. Physiol., Suppl.-Bd.*, 243, 1889.
- BEGG, R. C.: The urachus and umbilical fistulae. *Surg. Gynec. Obst.*, 45: 165, 1927.
- BEGG, R. C.: The urachus; its anatomy, histology, and development. *J. Anat.*, 64: 170, 1930.
- BELL, SIR CHARLES: Account of the muscles of the ureters and their effects on the irritable state of the bladder. *Trans. Med.-Chir.*, 3: 171, 1912.
- BOUILLIE, M.: L'Hypertrophie du col vésical. *J. d'uro.*, 27: 97, 1929.
- BRACELEY, E.: Extrophy of the bladder complicated by other genital anomalies. *Am. J. Diseases Child*, 43: 931, 1932.
- BRANDL, K.: Contribution to the study of ectopia vesicae. *Am. J. Urol.*, 9: 333, 1913.
- BREWER, G. E.: Extrophy of the bladder. *Ann. Surg.*, 57: 781, 1913.
- BROWN, DAMON A.: Patent urachus opening through solitary ulcer of the bladder. *J. Urol.*, 17: 509, 1927.
- CAMPBELL, M. F.: High-frequency resection of congenital vesical outlet obstruction in children. *J. Rec.*, 146: 26, 1937.
- CATHLIN, F., AND SEMPE, C.: La vessie double. *Ann. d. mal. d. org. génito-urin.*, 21: 339, 1903.
- CAULK, J. R.: Hour-glass bladder: resection of base of bladder for transverse septa. *Ann. Surg.*, 71: 22, 1920.
- CHEETHAM, J. G.: Clinical evaluation of the cystometer. *J. Urol.*, 39: 569, April 1938.
- CHWALLER, R.: Congenital hour-glass bladder. *Ztschr. f. Urol. Chir.*, 230: 200, 1927.
- CLOAKE, P. C.: Discussion on the innervation of the bladder. *Proc. Roy. Soc. Med.*, 25: 547, 1932.
- COLBY, F. H.: Patent urachus. *New England J. Med.*, 204: 900, April 30, 1931.
- CROSS, J. B.: Cysts of the urachus. *J. Urol.*, 33: 408, 1935.

- CULLEN, T. S.: Diseases of the umbilicus. Phila., W. B. Saunders Co., 1916.
- CUTLER: (Hour-glass bladder, 1854) Quoted by Eisenstaedt and McDougall.
- CZYBLARZ AND MARBURY: *Jahrb. f. Psychiat. u. Neurol.*, 20: 134, 1901.
- DAVIS, G. G. (revised by G. P. Muller): *Applied anatomy*. Ed. 6. Phila., J. B. Lippincott Co., 1924.
- DENNEEN, E. V., AND MARGOLD, A.: Patent urachus. *J. Urol.*, 25: 457 1931.
- DENNIG, H.: *Die innervation der harnblase, physiologie und klinik*. Heft 45, Gesamtgebete der Neurologie und Psychiatrie. Berlin, J. Springer, 1926.
- DENNY-BROWN, D., AND ROBERTSON, E. G.: On the physiology of micturition. *Brain*, 56: 149, 1933.
- DENNY-BROWN, D., AND ROBERTSON, E. G.: The state of the bladder and its sphincters in complete transverse lesions of the spinal cord and cauda equina. *Brain*, 56: 397, 1933.
- DETWEILER, E. L.: An hour-glass bladder. *Virginia M. Monthly*, 15: 644, 1888-89.
- DOUGLASS, M.: Urachal cysts and fistulae. *Am. J. Surg.*, 22: 557, 1933.
- DUCLAUX, H., AND BLONDIN, S.: L'ouraque et les fistules urinaires de l'ombilic. *Rev. de Chir.*, 51: 45, 1932.
- EISENSTAEDT, J. S., AND MCDUGALL, T. G.: True hour-glass bladder. etiology and treatment. *Arch. Surg.*, 32: 1007, 1936.
- ELLIOTT, T. R.: The innervation of the bladder and urethra. *J. Physiol.*, 35: 367, 1907.
- FARABEUF, L. H.: Les vaisseaux sanguins des organes génito-urinaires du périnée et du pelvis. (Amplification de la thèse du Dr. Leon Cerf). Paris, Masson et Cie, 1905.
- FEARNSIDES, E. G.: The innervation of the bladder and urethra; a review. *Brain*, 40: 149, 1917.
- FELIX, W.: Development of the urinogenital organs. Keibel-Mall, *Human Embryology*. Ed. 2. Phila., J. B. Lippincott Co., 1912.
- FENWICK, E. H.: The venous system of the bladder and its surroundings. *J. Anat. & Physiol.*, 19: 320, 1885.
- FRANKL-HOCHWART, L. VON, AND FROHLICH, A.: Ueber die corticale innervation der harnblase. *Neurol. Centralbl.*, 23: 646, 1904.
- FRIEDEL, A.: Die entleerung der harnblase nach Heiss. *Med. Klin.*, 25: 1396, September 6, 1929.
- FULLER, EUGENE: Antero-posterior subdivision of the bladder: an important anomaly. *J. Cutan. & Genito-Urin. Dis.*, 18: 531, 1900.
- GASKELL, W. H.: The involuntary nervous system. N. Y., Longmans Green & Co., 1920.
- GELDERN, C. E. VON: The etiology of exstrophy of the bladder. *Arch. Surg.*, 8: 61, 1924.
- GERNON, J. T., PALMER, E., AND MCKENNA, C. M.: Some recent developments in the treatment of neurogenic dysfunction of the bladder, based on cystometry. *J. Urol.*, 35: 515, 1936.
- GRANTHAM, W. L., AND BUNTS, R. C.: Congenital obstruction of the bladder neck. *Southern M. J.*, 33: 939, 1940.
- GREENBERG, GEZA: Vesica duplex, with gangrenous cystitis. *Urol. & Cutan. Rev.*, 40: 175, 1936.
- GRUBER, G. B., *et al.*: (Hour-glass bladder). *Handbuch der biologische*, P. 78 Berlin, J. Springer, 1928.
- HEISS (See Friedel).
- HENDERSON, V. E., AND ROEPKE, M. H.: The urinary bladder mechanisms. *J. Pharmacol.*, 51: 97, 1934.
- HERBST, W. P.: Patent urachus. *Southern M. J.*, 30: 711, 1937.
- HOLMES, GORDON. Observation on the paralyzed bladder. *Brain*, 56: 383, 1933.

- JOHNSTON, T. B.: Extroversion of the bladder, complicated by the presence of intestinal openings on the surface of the extroverted area. *J. Anat. & Physiol.*, 48: 89, 1914.
- JORDAN, H. E., AND KINDRED, J. E.: *A textbook of embryology*. N. Y., D. Appleton & Co., 1926.
- KEARNS, W. M., AND TURKELTAUB, S. M.: Hour-glass deformity of the urinary bladder. *J. Urol.*, 29: 729, 1933.
- KEIFFER: Anatomie vasculaire de la vessie et du col vésical. *Bull. Soc. belge de gynec. et d'obst.*, 9: 194, 1898-99.
- KEITH, A.: Three demonstrations on malformations of the hind end of the body. *Brit. M. J.*, 3: 1736, 1908.
- KRETSCHMER, H. L., AND MORRIS, H. L.: True hour-glass bladder: case. *J. Urol.*, 10: 181, 1923.
- LANGLEY, J. N., AND ANDERSON, H. K.: The innervation of the pelvic and adjoining viscera. *J. Physiol.*, 19: 71, 1895.
- LANGWORTHY, O. R., *et al*: A clinical study of the control of the bladder by the central nervous system. *Bull. Johns Hopkins Hosp.*, 58: 89, 1936.
- LANGWORTHY, O. R., AND KULE, L. D.: The encephalic control of tone in the urinary bladder. *Brain*, 56: 371, 1933.
- LAVANT 'HOMME, P.: Du diagnostic des tumeurs kystiques abdominales volumineuses et des kystes de l'ouraque en particulier. *Bruxelles-méd.*, 17: 820, 1937.
- LEARMONTH, J. R.: A contribution to the neurophysiology of the bladder in man. *Brain*, 54: 147, 1931.
- LEARMONTH, J. R.: Value of neurosurgery in certain vesical conditions. *J. A. M. A.*, 98: 632, 1932.
- LEARMONTH, J. R., AND BRAASCH, W. F.: Resection of the presacral nerve in the treatment of cord bladder. *Surg. Gynec. & Obst.*, 51: 494, 1930.
- LEWIS, L. G., LANGWORTHY, O. R., AND DEES, J. E.: Bladder abnormalities due to injury of the motor pathways in the nerves. *J. A. M. A.*, 105: 2126, 1935.
- LEWIS, L. G., AND LANGWORTHY, O. R.: Cystometry. *J. Urol.*, 40: 677, November 1938.
- LOWER, W. E.: Extrophy of the urinary bladder with carcinoma. *Ann. Surg.*, 73: 354, 1921.
- LOWSLEY, O. S., AND HUNT, R. W.: A new clinical cystometer. *Urol. & Cutan. Rev.*, 41: 545, 1937.
- MACALPINE, J. B.: The musculature of the bladder neck of the male in health and disease. *Proc. Roy. Soc. Med. (Sect. Urol.)* 28: 39, 1934.
- MACDONALD, A. D., AND MCCREA, E. D.: Observations on the control of the bladder; the effect of the nervous stimulation of drugs. *Quart. J. Exper. Physiol.*, 20: 379, 1930.
- MACKENZIE, D. W., AND HACK, S.: A new cystometer devised to minimize present difficulties. *J. Urol.*, 28: 131, 1937.
- MAHONEY, P. J., AND ENNIS, D.: Congenital patent urachus. *New England J. Med.*, 215: 193, 1936.
- MCCLEINTOCK, G. F.: The clinical neurophysiology of the automatic urinary bladder and enuresis. *J. Urol.*, 20: 267, 1928.
- MCCREA, E. D'ARCY: *The musculature of the bladder*. *Proc. Roy. Soc. Med. (Sect. Urol.)*, 19: 35, 1926.
- MCCREA, E. D., AND MACDONALD, A. D.: Presacral sympathectomy and the urinary bladder. *Brit. J. Urol.*, 6: 119, 1934.
- MCGOWN, P. E.: Carcinoma in extrophy of the bladder. *J. Urol.*, 43: 533, 1940.
- MEZAN, S.: Contribution à l'étude clinique de la vessie multiloculaire. *J. d'urolog.*, 27: 31, 1929.
- MOORHEAD, J. J. AND MOORHEAD, E. L.: Extrophy of the bladder: 2 cases. *J. A. M. A.*, 63: 409, 1916.

- MOSSO AND PELLACANI: (Quoted by Fearnside).
- MÜLLER, B.: Ein fall von missbildung am beckensteil des weiblichen urogenital apparatus. Inaug. Dissert., Marburg, 1895.
- MUNRO, DONALD: The activity of the urinary bladder as measured by a new and inexpensive cystometer. *New England J. Med.*, 214: 617, 1936.
- MUSCHAT, MAURICE: A study of the response of the trigone and detrusor musculature to vesical neck obstruction. *J. Urol.*, 30: 221, 1933.
- MUSCHAT, MAURICE: Simplified interpretations of cystometrograms. *J. Urol.*, 34: 340, 1935.
- MUSCHAT, M., AND JOHNSON, C. C.: A simple and inexpensive cystometer. *J. Urol.*, 27: 273, 1932.
- MUSCHAT, M., *et al.*: The normal cystometrogram. *J. Urol.*, 37: 718, 1937.
- NESBIT, R. M., AND BROMME, W.: Double penis and double bladder. *J. Roentgen.*, 30: 497, 1933.
- ORTMANN, K. K., AND CHRISTIANSEN, H.: Roentgenographic studies of the male urethra; the closing mechanism of the bladder, etc. *Acta Radiol.*, 15: 258, 1934.
- PAGENSTECHER, E.: Ueber entstehung und behandlung der angeborenen blasendivertikel und doppelblasen. *Arch. f. Clin. Chir.*, 74: 186, 1904.
- PASSOW: (Hour-glass bladder, 1848) Quoted by Caulk.
- PATEL, M., AND LABRY, A.: Large closed cysts of the urachus. *Genec. et Obstet.*, 12: 449, 1925. *Abstr. J. A. M. A.*, 86: 1169, 1926.
- PAYNE, R. L., AND JONES, JR. R. D.: Carcinoma of the urachus: 2 cases *Virginia M. Monthly*, 58: 90, 1931.
- PHÉLIP, L.: Recherches endoscopiques sur le fonctionnement du col vésical et les retentions inéomplètes. *Lyon méd.*, 131: 203, 1922. Also: *Lyon chir.*, 19: 171, 1922.
- POHLMAN, A. G.: The development of the cloaca in human embryos. *Am. J. Anat.*, 12: 1, 1911-12.
- PRENTISS, C. W.: A laboratory manual and textbook of embryology. Phila., W. B. Saunders Co., 1915.
- REDEWILL, F. H.: The physiology of micturition, etc., *J. A. M. A.*, 91: 1960, 1928.
- RIEDER, W.: Total offener urachus von aussergewöhnlicher grosse und seine behandlung. *Ztralb. f. Chir.*, 61: 882, 1934.
- ROSE, D. K.: Determination of bladder pressure with the cystometer. *J. A. M. A.*, 88: 151, 1927.
- ROSE, D. K.: Clinical applications of bladder physiology. *J. Urol.*, 26: 91, 1931.
- ROSE, D. K.: Improved continuous-flow recording cystometer. *J. Urol.*, 43: 718, 1940.
- SCHMIDT, C. B.: Misbildungen und erkrankungen am urachus. *Med. Kln.*, 29: 702, May 19, 1933.
- SHERINGTON, C.: Notes on the arrangement of some motor fibers in the lumbosacral plexus. *J. Physiol.*, 13: 621, 1892.
- SIMEONE, F. A., AND LAMPSON, R. S.: A cystometric study of bladder function. *Ann. Surg.*, 106: 413, 1937.
- SIMONS, I.: Cystometry: its status and outlook. *Urol. & Cutan. Rev.*, 42: 316, May 1938.
- SIMONS, I.: Cystometry: studies in bladder function. No. 6: A critical review with special reference to microcystometry and sphincterometry. *Brit. J. Urol.*, 9: 132, 1937.
- SIMONS, I., AND EMANUEL, M.: The neuro-anatomy and neuro-physiology of the bladder. *Urol. & Cutan. Rev.*, 44: 102, 1940.
- SPALTEHOLZ, WERNER (Trans. Barker, L.): Human anatomy, Vol III. Ed. 7. Phila. J. B. Lippincott Co., 1923.
- TRUMBLE, H. C.: Experimental reinnervation of the paralyzed bladder. *Med. J. Australia*, 1: 118, 1935.

- TSAKNIS, DENIS: Les pedicules vasculaires de vessie et son péritoine chez l'homme. Arch. d. mal. d. reins et d. organes génitaux-urinaires, 4: 442, 1929.
- VALENTINE: (Quoted by Fearnside).
- VAUGHAN, G. T.: Patent urachus: review of cases; operation; tumors and cysts. Trans. Am. Surg. Assoc., Phila., 23: 273, 1905.
- WALLACE, W. J.: Unusual bladder obstruction. J. Urol., 15: 325, 1926.
- WESSON, M. B.: Anatomical, embryological, and physiological studies of the trigone and neck of the bladder. J. Urol., 4: 279, 1920.
- WESSON, M. B.: Anatomical variations of the bladder. In "The Encyclopedia of Med. Surg., and Specialties." Phila., F. D. Davis Co., 1939.
- WEYRAUCH, H. M., JR.: A simplified cystometer, etc. J. Urol., 35: 103, 1936.
- WILMOTH, C. L.: Persistent urachus in adult. J. A. M. A., 106: 526, February 15, 1936.
- WOOD-JONES, F.: Extroversion of the bladder and some problems in connection with it. J. Anat. & Physiol., 46: 193, 1912.
- WYBURN, G. M.: The development of the intra-umbilical portion of the abdominal wall, with remarks on the etiology of ectopia vesicae. J. Anat., 71: 201, 1937.
- YOUNG, H. H.: Exstrophy of the bladder. Surg., Gynec. & Obst., 74: 729, 1912.
- YOUNG, H. H. AND DAVIS, D. M.: The practice of urology. Phila., W. B. Saunders Co., 1926.
- YOUNG, H. H., AND MACHT, D.: A contribution to the physiology and pharmacology of the trigonum vesicae. J. Pharmacol. & Exper. Therap., 22: 329, 1923.
- YOUNG, H. H., AND WESSON, M. B.: The anatomy and surgery of the trigone. Arch. Surg., 3: 1, 1921.



CHAPTER XXXI

INJURIES AND DISEASES OF THE BLADDER

A. INJURIES TO THE BLADDER

Injuries to the urinary bladder are relatively infrequent, due to its protected situation in the bony pelvis. Most vesical injuries occur during distention of the bladder, when it arises above the symphysis pubis and becomes an abdominal organ, in which state it is much more subject to trauma.

Bladder injuries are of three types: (1) contusions, due to kicks, falls, etc., which are seldom diagnosed and are of slight clinical importance, although rarely they may be serious enough to cause death by shock and hemorrhage; (2) wounds, usually communicating with the exterior, due to puncture or perforation by sharp or blunt objects; (3) rupture—by far the most common injury.

Wounds of the Bladder

Etiology. Wounds of the bladder are encountered very infrequently in civil practice, and belong primarily to the realm of war surgery. They are produced chiefly by bullets or by pointed instruments, such as sabers, bayonets, knives, or fragments of shell or shrapnel. During the First World War such injuries were fairly frequent and were inflicted, as a rule, by shrapnel. In civil practice, the bladder is occasionally injured accidentally during surgical operation or urethral instrumentation. Perforation of the bladder wall by a fragment of bone may occur in fracture of the pelvis.

Pathology. Bladder wounds may be very slight or extensive, depending upon the size of the penetrating object. They may be either intraperitoneal or extraperitoneal. The former are the more serious as a rule. Vesical wounds associated with injuries to the buttocks, perineum, or thighs are more likely to be extraperitoneal, while those inflicted through the abdomen are usually intraperitoneal. Such wounds may be uncomplicated, but usually the surrounding structures are involved to some extent. In war injuries or pelvic fractures, the associated injuries

to the neighboring viscera, bones, and large blood vessels may be very extensive.

Symptoms. The symptoms and course vary greatly in wounds of the bladder, depending upon the extent of the wound, its location (whether intraperitoneal or extraperitoneal), and the associated injuries. Shock is likely to be present in some degree, and may be very severe; but cases of serious traumatization have not infrequently been reported in which shock or other early indications of bladder injury were trifling or wholly absent.

Hemorrhage may be so severe as to prove rapidly fatal; or the detection of blood in the urine which the patient is able to void normally may be the first indication that the bladder has been injured.

The most common early symptoms suggestive of bladder injury are pain in the hypogastrium, more or less shock, and a constant desire to void and inability to do so, or the passage of a small amount of blood-stained urine. Escape of blood-stained urine through the wound is, of course, conclusive proof of penetration of the bladder. However, the urine may extravasate into the perivesical tissues or leak into the peritoneal cavity. With the extravasation of urine, the abdomen becomes distended, rigid, and tender, or the urine may extravasate extraperitoneally and form a palpable mass in one or both flanks. If the wound involves the peritoneum, there will be free fluid in the abdominal cavity. These symptoms, however, are not usually in evidence until several hours after the accident.

Diagnosis. Early diagnosis and surgical repair are of the utmost importance, since urinary extravasation and subsequent infection are the chief dangers in those cases which survive the initial shock and hemorrhage.

Penetrating wounds of the bladder are always to be suspected in wounds involving the hypogastrium, buttocks, and perineum. The direction and extent of all such wounds should be very carefully studied, bearing in mind the possibility of injury to the bladder and the gravity of such injury when it does occur. In wounds involving the buttocks, particularly, associated extraperitoneal wounds of the bladder have not infrequently wholly escaped discovery. Wounds near the vesical neck are most likely to escape notice because of the difficulty of examining this area with the ordinary cystoscope. If some time has elapsed between the receipt of the injury and the examination, the swelling and

edema, or hemorrhage, may make it impossible to see the wound. In very severe injuries, cystoscopy is, of course, impossible.

Sometimes the history and physical examination are sufficient to establish the diagnosis without instrumentation. Catheterization, cystoscopy, and injection cystography and aerograms are all valuable in making the diagnosis and in ascertaining the location and extent of the wound, but their use is always accompanied by the risk of increasing the incidence of infection, and in extensive injuries may be out of the question. Excretory cystograms are very useful, if sufficient time for this procedure can be allowed; and the danger of infection is less by this method. All of these methods are discussed under the diagnosis of rupture.

Treatment. The treatment consists of supportive measures and surgical repair at the earliest possible moment after the diagnosis has been made, with drainage of the bladder and of the infiltrated areas if extravasation has occurred. The surgical treatment is substantially the same as that of rupture, and is described under Surgical Treatment of Bladder Wounds and Ruptures (p. 1120).

Rupture of the Bladder

Etiology. The usual cause of rupture of the bladder is some external violence to an overdistended viscus. Alcoholism is one of the most important factors predisposing to bladder rupture, since it is in the intoxicated state that the bladder is often subjected to overfilling, and this, together with the associated relaxed condition of the abdominal muscles, renders it more susceptible to injury. Other predisposing causes are vesical distention from any cause; chronic conditions (enlarged prostate, urethral stricture) causing urinary retention; and disease of the bladder (inflammation, ulceration, atony, diverticula). Spontaneous rupture and rupture from muscular effort have been reported, but invariably in these cases there is some accessory factor, such as overdistention or disease, which has produced weakening of the bladder wall. Rupture of the bladder is frequently associated with crushing injuries involving fracture of the pelvis (25 out of 166 fracture cases, Campbell; 65 out of 169 cases, Bartels). The incidence of such cases is increasing with the increase of automobile accidents. Rupture or perforation sometimes occurs from extravescical pathological processes.

Occasionally rupture may be secondary to instrumentation or surgical manipulations. It may occur from overdistention with irrigation fluid

at cystoscopy, in which event there will usually be found a pathological weakening of the wall; or the wall may be penetrated by the cystoscope, lithotrite, or other instrument; or there may be too deep fulguration of a tumor or ulcer. In recent years extraperitoneal ruptures at the vesical orifice, caused by the electrical loop in vesical neck resection, have been reported.

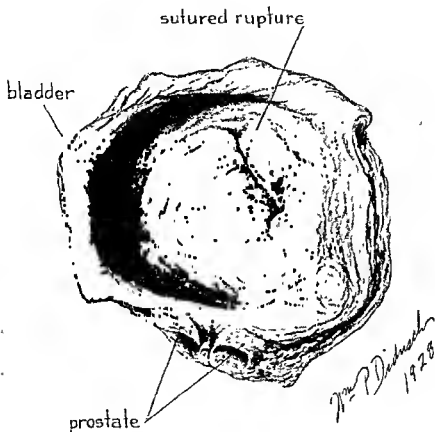


FIG. 222. Rupture of tabetic bladder. (From the collection of the late Dr. E. Christeller, Virchow's Krankenhaus, Berlin.)

Pathology. Rupture of the bladder may be either intraperitoneal or extraperitoneal, or may partake of the nature of both classifications.

Intraperitoneal ruptures are more frequent than extraperitoneal ones, due, probably, to the fact that the usual trauma is to the anterior abdominal wall and occurs when the bladder is distended. When the bladder is only partially filled, extraperitoneal rupture is more frequent.

The site of intraperitoneal rupture is usually on the postero-superior aspect, which is the least supported and most vulnerable portion of the bladder. Extravasation of urine into the peritoneum rapidly follows, making early surgical intervention imperative.

Extraperitoneal rupture is most likely to occur in conjunction with fracture of the pelvis. It results from severe violence directed against the hypogastrium or perineum, and, when this violence is simultaneously exerted in both these directions, the bladder has small chance of escaping serious injury. The most frequent site of extraperitoneal rupture is in the trigonal area. Occasionally the tear may be in the preperitoneal tissues in front, the space of Retzius, or in the side of the vesical neck. With fractured pelvis, the bladder may either rupture or, if the bones have been splintered, be perforated in one or more places by fragments of bone. Perforation is more likely to occur with a distended bladder, but may happen also with a comparatively empty one.

Symptoms. Both the intraperitoneal and extraperitoneal types of rupture give similar symptoms, but the manifestations in the former type are usually more severe, and, in addition, there are likely to be symptoms of peritonitis, unless the patient is seen early.

In *intraperitoneal rupture*, the common early symptoms are shock, which may be slight or so severe as to cause death; pain and tenderness in the hypogastrium; and a marked desire to void, with inability to do so or, at most, the passage of a few drops of blood. Occasionally there may be ability to void immediately after the accident, but evacuation will be painful and the urine blood-stained. The abdominal distention, rigidity, and tenderness increase with the extravasation of urine, but gastrointestinal symptoms are usually absent until peritonitis develops. If the urine is infected at the time of injury, the later symptoms are those of a septic peritonitis.

In *extraperitoneal rupture*, early symptoms may be few or entirely lacking. If incurred in association with fracture of the pelvis, the symptoms produced by the latter may temporarily mask the manifestations of the vesical injury, and it is only when the extravasated urine has had time to burrow into the surrounding tissues that the gravity of the bladder injuries is manifested. With subsequent infection, the clinical picture becomes that of sepsis. The pain following extraperitoneal rupture may be localized in the suprapubic region or referred to the perineum, rectum, penis, or lower extremities. There may be the passage of blood-stained urine, or total inability to void. If the site of the rupture

is in the base of the bladder, the urine will usually extravasate first into the most dependent part of the extravescical space, that is, the region occupied by the seminal vesicles behind the prostate, and, even if the rupture is higher up, the fluid will later invade this area. Its course may be upward, behind the posterior parietal peritoneum, in which case a mass may be palpated above the iliac crest or in one or both loins. In some instances there has even been invasion of the thigh, the extravasating urine dissecting under Poupart's ligament, generally externally to the internal iliac vessels; or it may reach the scrotum, along and externally to the structures occupying the inguinal canal. Extravasations can penetrate the pelvic fascia into the ischiorectal space and perineum, but this is unlikely unless the trauma causing the bladder rent has also caused disruption of other structures which normally would act as natural barriers.

Diagnosis. Intraperitoneal rupture, in particular, frequently takes place without any associated injuries. In little children, especially, the diagnosis may be very difficult, because rupture of the bladder is a rare condition in childhood and the possibility of its occurrence is likely to be overlooked. However, young patients as well as older ones may be caught unawares with a full bladder, and even a trivial fall, as from a toy wagon, may be sufficient to cause vesical rupture.

The history and physical examination are very important. A history of injury to the lower part of the abdomen, followed by hypogastric pain and intense desire to void with inability to do so, or by the passage of bloody urine, should make one suspect rupture of the bladder. The presumption of rupture is strengthened by the presence of a palpable mass in the lower abdomen or in the retrovesical region, or by free fluid in the abdomen, but these are later manifestations and to wait for their appearance is likely to prove disastrous.

Where bladder injury is suspected, the patient should be requested to empty the bladder. His ability to pass urine which is not macroscopically bloody will be a fairly reliable indication that the bladder is intact.

The most commonly employed diagnostic procedure has been catheterization. Its use confirms an empty bladder or the presence of a small amount of bloody urine. Another method is to instil a measured quantity of sterile fluid and immediately attempt to withdraw it. If the amount recovered is less than that introduced, rupture should be suspected. Cystoscopy is sometimes useful in demonstrating the presence

and location of small ruptures; but in larger tears, the inability to keep the bladder sufficiently distended, and the excessive bleeding, may make determination of the injury impossible. In many cases the associated injuries and the patient's general condition make cystoscopy entirely out of the question. Injection cystography and aerograms are also of value in demonstrating injury. However, neither a catheter nor a cystoscope can be passed without risk of additional traumatization and increase in the incidence of infection. Where the necessary time for the procedure can be allowed, diagnosis is best made by intravenous urography, which permits secretory cystograms showing the diffused dye outside the bladder. This procedure lessens the danger of infection. Because of the frequency of associated bladder injury, all cases of fractured pelvis should have early intravenous urographic study unless the patient can pass normal quantities of urine.

Immediate exploratory operation, preceded by a transfusion, if necessary, is advisable in all cases where the diagnosis is in doubt but where the history and findings indicate rupture. Rupture of the bladder, particularly the intraperitoneal variety, requires emergency surgery, and a favorable outcome is dependent upon the length of time that elapses between receipt of the injury and institution of efficient drainage.

Prognosis. The prognosis, particularly in intraperitoneal rupture, is grave. The primary shock and hemorrhage may be so severe as to be rapidly fatal; or death may occur from peritonitis, rapid sepsis due to early infection developing in the extravasated tissues, or from associated injuries. Early recognition and repair are of primary importance. The high mortality in intraperitoneal ruptures has been largely due to failure to recognize the condition early enough for operation to be performed before infection has set in. Extraperitoneal ruptures, if uncomplicated, are usually less dangerous. An increasing proportion of these cases, however, are associated with fracture of the pelvis and extensive injury to adjacent structures.

The mortality of rupture of the bladder is necessarily dependent in part upon the extent of general injuries, but it can be materially reduced by early diagnosis and operation.

Treatment. The treatment consists of supportive measures, such as infusions or transfusions, external heat, and stimulants, and emergency surgery for drainage, diversion of the urinary stream, and repair of the bladder in accordance with the findings. The latter is described under *Surgical Treatment of Rupture and Wounds of the Bladder* (p. 1120).

Radium and X-ray Burns of the Bladder

Injuries to the bladder following radiation have received almost no consideration in urological textbooks. Injury to the bladder base may follow radium or roentgen therapy of the prostate, uterus, or other pelvic organs. A. L. Dean (1933) reported 47 cases of bladder burns following irradiation of the uterus, and states that the possibility of vesical injuries must be recognized by all physicians who treat uterine diseases. In some cases the bladder injury followed comparatively light doses of radiation to benign uterine lesions.

The bladder lesion is a form of obliterative endarteritis, resulting in necrosis of the tissues. It is usually found in the posterior third of the bladder base and in most cases is confined to the mucous membrane, indicating that the mucosa is more sensitive to radiation than the underlying interstitial and muscular tissue.

Symptoms and Diagnosis. As a rule, a considerable period of time elapses between the radiation and the development of vesical symptoms (from 1 to 10 years or more). The onset of symptoms is usually sudden. Frequency, dysuria, and hematuria, which may be profuse, are the common bladder symptoms.

Cystoscopic examination shows a central necrotic area surrounded by a zone of edema, or an anemic grayish area surrounded by a red telangiectatic zone. Infection is always present, and the ulcerations are often covered with encrustations.

The diagnosis is based upon the history, cystoscopic picture, and a biopsy by means of the cystoscopic rongeur. A history of frequency, dysuria, and hematuria, with previous uterine, prostatic, vesical, or other pelvic disease treated by irradiation, should suggest the possibility of a tertiary radiation reaction. The diagnosis is not easy, since the cystoscopic picture may resemble that of vesical carcinoma, encrusted cystitis, or Hunner's ulcer. In carcinoma the growth usually rises abruptly from the mucous membrane, and normal mucous membrane can be seen extending up to the tumor's edge, whereas in radium burns the mucous membrane for quite a zone around the central lesion shows edema and redness (Smith). The only definite means of diagnosis is by biopsy, and this is always indicated. Dean warns of the dangers of treating radiation injuries of the bladder by radiation, fulguration, or any other destructive method employed in the treatment of cancer, and of the possibility of producing fistulas. Since these lesions are apparently of

fairly frequent occurrence, the urologist should be familiar with them and should always bear in mind the possibility of radiation burns in the differential diagnosis of vesical lesions.

Prognosis. In a few cases death has resulted from profuse secondary hemorrhage following ulceration. In other cases there has been extensive destruction of tissue. In the majority of cases, however, the end-results, with proper treatment, are excellent, although treatment may have to be persisted with over a period of many months.

Treatment. The best results have been obtained by acidifying the urine (which is usually of alkaline reaction), daily lavage of the bladder with phosphoric acid, beginning with a 1 per cent solution and increasing to 5 per cent, and daily instillations of argyrol. Sedatives may be necessary for the relief of pain, which is sometimes intense.

Injuries to the Female Bladder Sustained During Parturition

During a prolonged labor, or one necessitating much instrumentation, the bladder may be injured by pressure of the fetal head as it passes through the portion of the vaginal canal in contact with the bladder base; or it may be bruised by forceps inexpertly applied. By irreparably damaging the blood vessels, such trauma interferes with nutrition of the parts, resulting, in the more serious cases, in sloughing of the tissues and the formation of fistulas between the urinary and genital tracts. Occasionally the bladder may be pierced by an instrument. Rupture of the bladder during labor is, however, very rare.

Vesicovaginal and other urinary fistulas, which may follow a difficult labor, trauma, or some gynecological operation, such as vaginal hysterectomy, are considered under Vesical Fistulas, (p. 1076).

B. DISEASES OF THE BLADDER

Cystitis

By "cystitis" is meant an inflammation of the urinary bladder characterized by frequent and painful urination and pus in the urine. Inflammations of the bladder are very common. They are usually secondary to lesions elsewhere in the urogenital tract or in the gastrointestinal tract (fissure, hemorrhoids, diverticulitis, carcinoma of the rectum or colon), or to general disease processes (diabetes mellitus, nephritis, tabes dorsalis) or foci of infection. Cystitis as a primary lesion is rare.

Inflammations of the bladder may be acute or chronic, and of non-bacterial origin or caused by specific or non-specific organisms.

Wm. P. Diduch

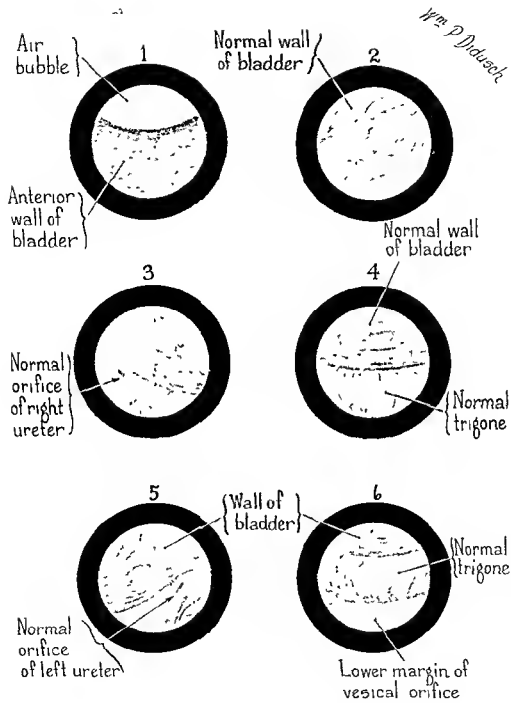


PLATE I. THE NORMAL BLADDER AS VIEWED THROUGH THE CYSTOSCOPE

Etiology. Bacterial Causes. Bacterial or parasitic invasion is the most common cause of vesical inflammation. The agents that may be responsible include all of the ordinary pathological organisms, but bacillary infections due to the colon bacillus predominate. The colon bacillus has numerous strains, which vary in toxicity. Seventy-five per cent or more of colon bacillus infections of the urinary tract are due to organisms of the true *B. coli* group (*Escherichia*). Next in frequency in bladder infections is the staphylococcus. Other organisms are streptococci, colon bacilli of the aerogenes group, and bacilli of the proteus and pyocyaneus groups. The *Micrococcus catarrhalis* and pneumococci are uncommon.

Specific organisms include the gonococcus, Koch's bacillus, *Spirochaeta pallida*, *Schistosoma haematobium*, *actinomyces*, various forms of amebae, the *Taenia echinococcus*, and the *Trichomonas vaginalis*. The vesical inflammations produced by these specific organisms are described under their respective headings.

The specific organisms of certain infectious diseases, such as influenza, typhoid fever, meningitis, and dysentery, are also found in the bladder.

Mixed infections are very common.

Non-Bacterial Causes. Chemical irritation may set up inflammation of the vesical mucosa. Overindulgence in alcoholic beverages, especially beer, the ingestion of cantharides or urinary antiseptics in too large quantities, exposure to turpentine, coal-tar products, and other irritating chemicals, the injection into the bladder of strong chemicals, hyperacid or ammoniacal urine—any one of these may cause inflammation of the bladder. Chemical substances derived from the food and excreted in the urine may cause vesical irritation.

Mechanical irritation of the mucosa, due to the presence of a calculus, a foreign body introduced by the patient or his physician (retention, catheter, etc.), a necrotic bladder tumor, or an extravescical mass, may cause cystitis.

Postoperative, Pregnancy, and Postpartum Cystitis. Postoperative and postpartum inflammations of the bladder are frequent, but pregnancy cystitis is relatively uncommon.

Postoperative cystitis may follow practically any intervention upon the urinary tract, and frequently occurs after hysterectomy and other gynecological operations, as well as after interventions upon more remote organs. Postoperative cystitis is often extremely obstinate in yielding to treatment, and it is hardly necessary to state that the best treatment of these

conditions is preventive. Prevention is often possible in postoperative cases, where the patient can be made to void without catheterization. When catheterization is necessary, soft catheters and the strictest aseptic technic should be used. Postoperative cases, however, should not be allowed to remain too long with overdistended bladders. In operations upon the prostate and bladder, especially, adequate preoperative attention will largely obviate postoperative cystitis. A vigorous course of treatment aimed at the elimination of pyogenic organisms from the bladder and urethra should be an indispensable part of the routine preoperative preparation.

Cystitis in pregnancy is relatively infrequent. When it does occur, it is usually secondary to a pyelitis or the result of traumatic injury or infection through unwise catheterization. Crabtree, who has made extensive urological studies of pregnant women at the Boston Lying-In Hospital, found that, in general, the bladder of the pregnant woman shows great tolerance to infective agents, and cystitis is rarely encountered even in bladders through which purulent urine from a diseased kidney has been passing for months. Retention of urine may occur during pregnancy from retroversion of the gravid uterus at about the end of the third month, or from pressure of the fetal head in the later months. Overdistention and residual urine eventually bring about cystitis. This can best be remedied by placing the fetus in a normal position, using external manipulation. Catheterization is to be avoided if possible.

Whatever the cause remotely responsible for a pregnancy cystitis, the immediate agent is a pyogenic organism—usually the *Bacillus coli* or the *Staphylococcus pyogenes aureus*. If the vesical mucosa is intact, these organisms have no deleterious effect, but otherwise they are capable of great damage. Although the catheter is their most common means of entrance, it is probable that infective organisms also migrate upward through the urethra without instrumental intervention. In many cases there has doubtless been a preëxisting cystitis, possibly unknown to the patient, which is exacerbated by the pressure of the enlarging uterus or reactivated by injudicious diet, instrumentation, or disease in the upper urinary tract.

The elimination of any mechanical causes, with rest in bed, bland diet, and alkalization and dilution of the urine, with avoidance of instrumentation, will generally clear up the cystitis.

In *postpartum cases*, the symptoms of cystitis, which are recognized to be very deceptive while pregnancy is in progress, appear to play a more

important part (Crabtree)., Frequently a urinary-tract infection will be more or less active for six months, or even a year, after delivery before any symptoms of cystitis will appear. The reason for this is not clear; but the importance of observing the woman who has had urinary-tract irregularities during pregnancy, for many months after delivery, is abundantly demonstrated. The treatment of postpartum cystitis is along the same lines as for general cystitis.

Routes of Invasion. Most vesical inflammations are secondary to infections of the urogenital tract either below or above the bladder. Invasion by way of the urethra, either as a result of instrumentation or by direct extension, is very common. In the female, in particular, infection may readily ascend to the bladder, due to the shortness of the urethra and the poor development of the external sphincter; and urethrocystitis and urethrotrigonitis are common complaints in females of all ages. Invasion of the bladder, following a prostatoseminal vesiculitis in the male or a cervicitis in the female, occurs frequently. Descending extension through the ureter, from a primary source in the upper urinary tract, is also very common in both sexes. Occasional portals of infection are the urachus and operative or spontaneous fistulas. Direct extension from a neighboring focus, such as an inflamed appendix, sigmoid, or oviduct, may occur. It is the opinion of most observers that the bladder is rarely directly invaded by means of the blood stream, which is so important in renal infections.

Since most vesical inflammations are secondary, the cause of the bladder lesion must be sought in every case.

Factors Predisposing to Cystitis. The normal urinary bladder has excellent defenses against bacterial invasion and is very resistant to infection. Bacteria do not readily penetrate its wall, and the external and internal sphincters are barriers to ascending infection from below. That bacteria may be introduced into the normal bladder without producing infection is a fact well known. This resistance of the bladder is probably due to its pavement epithelium, few glands, and the fact that it completely empties itself at frequent intervals. An infected bladder attempts to rid itself of its abnormal contents by increased activity (frequency); hence, infections in the normal bladder tend to disappear shortly unless there is an extravesical focus to feed organisms into it.

When a cystitis persists for more than two weeks, there is usually present either (1) an outside source for the continuous feeding of organisms into the bladder, (2) an obstruction to free urinary evacuation,

resulting in the presence of residual urine—an excellent culture medium, or (3) some factor, such as a vesical calculus or necrotic malignant tumor, producing constant mechanical irritation of the vesical mucosa.

Mechanical obstruction, resulting in more or less urinary retention, is a very common predisposing factor in vesical infection. Such obstruction may be due to a variety of causes, both congenital and acquired: phimosis; urethral stricture, diverticulum, stone, or tumor; urethrocele; posterior urethral valves; hypertrophy of the verumontanum, prostate, vesical neck, or interureteral ridge; prostatic carcinoma; median bar; contracture of the vesical neck; cystocele; and vesical diverticulum. The presence of any one of these may explain an intractable cystitis.

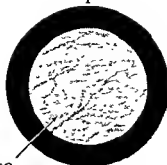
Lesions of the central or peripheral nerves, causing atony of the bladder and retention, are accessory factors in the production of cystitis.

Cure of the cystitis is dependent upon the removal of these sources of infection, obstruction, or traumatism.

Pathology. The mild form of cystitis, often termed *catarrhal*, usually is confined to the trigonal region or around the ureteral orifices. If left untreated, however, this may quickly progress to a more severe *interstitial* form (Plate II), involving a considerable extent of the bladder wall, which becomes thickened and edematous, often passing on to the formation of granulations, bullae, cysts, and even ulceration. Under these circumstances, the capacity of the bladder may be greatly reduced.

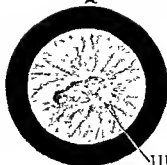
Acute Cystitis. In acute cystitis the glistening "peach-blossom" appearance of the normal vesical mucosa changes to a reddish blush. The delicate network of blood vessels, which normally is clearly discernible, is blotted out by engorgement of the capillaries. The inflammation may be diffuse or, in less severe cases, may be confined to certain areas, giving the mucosa a blotchy appearance. Markedly dilated blood vessels are to be seen in the mucosa. (See Plate II.) The most frequently affected portions of the bladder are the trigone and the floor of the vesical orifice—that is, the parts of the wall surrounding the portals through which infection usually enters the viscus. At points of intense inflammation there may be areas of superficial ulceration and ecchymoses. Often the edema is so marked, particularly about the vesical orifice, as to produce small bullae, which may become so aggravated as to cause the trigonum to resemble a bunch of grapes. In very severe cases the surface of the mucosa becomes shaggy, and strings of fibrin, muco-pus, and necrotic tissue may be seen clinging to it. Ulceration follows this state, and may infiltrate the musculature.

1



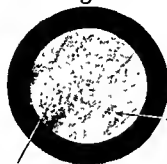
Cystitis

2



Ulcer

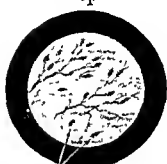
3



Ulcer with
encrustations

Orifice
of left
ureter

4



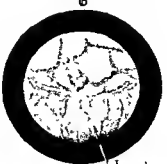
Hemorrhages along
course of arteries

5



Interstitial cystitis
Cracks
in mucosa following distention
of bladder

6



Leukoplakia

The inflammatory changes in acute cystitis are usually confined to the mucosa and submucosa. The mucous membrane is freely movable on the underlying muscle, which is uninvolved by the inflammatory process, although it may be somewhat hypertrophied from the increased activity caused by the vesical irritability.

Chronic Cystitis. Chronic cystitis is always interstitial, involving all the layers of the bladder wall. It is often accompanied by pericystitis. The capacity of the bladder is diminished, due to thickening of its wall and loss of its normal distensibility.

The mucous membrane has a dull, grayish appearance, and areas of dilated blood vessels and vascular ecchymoses may be seen, particularly in the trigone. It is rare to see the entire mucous membrane of the bladder equally involved in chronic cystitis. The mucosa loses its smoothness and is frequently more or less covered with projections. One of the commonest forms assumed by chronic cystitis is bullous edema (Plate VII), which is often met with in tuberculosis and sometimes in long-standing colon bacillus infection. Ulceration is a later manifestation of long-standing infection and often follows bullous edema. The ulcerations are sometimes encrusted with urinary salts (Encrusted Cystitis, p. 1011). In other cases, the mucosa is covered with a pseudomembranous exudate. Exceptionally, gangrenous cystitis is seen, usually as the end-result of a severe cystitis due to trauma and infection which have interfered with the blood supply. Cornification of the epithelium in spots may occur in long-standing cases. Trabeculations and diverticula are often present.

The mucosa is partly or completely desquamated, and there is inflammatory infiltration of the submucosa and, eventually, of the musculature. Multiple small interstitial hemorrhages are often seen (Plate II). The submucosa loses its flexibility and fuses with the musculature. Eventually, both the submucosa and the interfascicular interstitial tissue are replaced by dense sclerotic tissue. Later on, the muscle bundles themselves may be involved in the sclerotic process, resulting in more or less muscular atrophy.

Particular forms of cystitis may occur during the course of a chronic cystitis as the result of special changes in the mucosa.

(1) *Cystitis granulomatosa* is a common accompaniment of both chronic and encrusted cystitis. The vesical mucosa is more or less covered by exuberant granulation tissue, rich in blood vessels, which may occur in localized plaques or be diffuse (granular cystitis). These

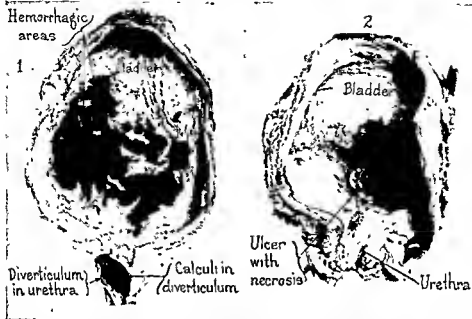


FIG. 223. (1) Cystitis, with large hemorrhagic areas present. There is a diverticulum in the urethra containing 5 stones. Female, aged 64 years. (2) Specimen of bladder showing a large ulcer on the posterior wall surrounded by a hemorrhagic area and with necrosis in the center. The collateral vessels are greatly injected. Female, aged 30 years. (Christeller.)

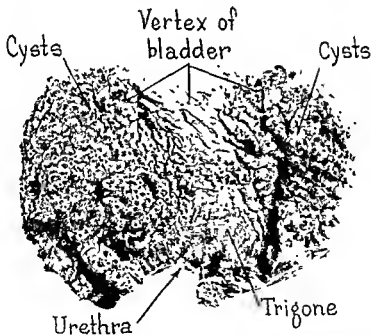


FIG. 224. Very extensive cystitis cystica. The only portion of the bladder which is free of cysts is the trigone. Specimen from a female, aged 59 years. (Christeller.)

papillary projections may be either single or grouped. They sometimes have a sessile appearance and may then resemble a neoplasm. They are true granulation tissue.

(2) *Cystitis glandularis* is a glandular proliferation due to chronic inflammation, the histological features suggesting that found in the small intestine. Occlusion of the glands may result in the formation of cysts. It occurs in the vesical mucosa of all long-standing cases of exstrophy of the bladder (Hinman).

(3) *Cystitis follicularis* is characterized by collections of rounded, yellowish nodules of lymphoid tissue, of varying number and size, with a surrounding red zone. The nodules may be so closely grouped as to appear confluent. Usually the overlying epithelium is intact. It is due to a subepithelial round-cell infiltration and lymph accumulation.

(4) *Cystitis cystica* is characterized by small groups of minute, round, translucent cysts, chiefly about the trigonal orifices. Cystoscopically, they are difficult to differentiate from certain types of bullous edema. The cysts lie in or directly beneath the mucosa, are lined with epithelium, and are filled with clear fluid resembling colloid. This type of lesion is also found in the ureter and renal pelvis (ureteritis cystica; pyelitis cystica).

(5) *Cystitis emphysematosa*—the presence of gas-containing vesicles in the bladder in association with inflammation—is chiefly an autopsy finding. It was formerly believed to be very rare and to occur almost exclusively in females. Only about 35 cases have been reported. Mills (1930) reported 11 cases found at autopsy at the Mayo Clinic, and stated that "cystitis emphysematosa is a distinct pathological entity and sooner or later it will be observed antemortem." In 1932, Ravich and Katzen reported the first authentic case observed *in vitam*. This was discovered at an emergency cystostomy, the patient making a complete recovery. Cases have subsequently been recorded by Redewill, Sanes and Doroshov, and Rosedale—in all of which the diagnosis was made postmortem. Wells (1938) reported 7 typical cases found in 1,800 routine necropsies between the years 1930 and 1938. The later reports indicate that this lesion is not so rare as was formerly believed, and that it occurs in men almost as often as in women.

In a typical case, the bladder wall, particularly in the trigonal region, is covered with multiple submucosal, clear, gas-filled vesicles protruding well into the vesical mucosa. The vesicles vary in diameter from 1 to 8 mm., are thin-walled, and lined with endothelium. Some are well rounded, while others are clefts produced by gas infiltration of the con-

nective tissue spaces (Wells). The intervening stroma contains polymorphonuclear leukocytes and, beneath them, hemorrhagic areas.

Nothing definite is known of the etiology. The condition has never been observed cystoscopically, and, with the exception of Ravich and Katzen's case, all of the reported cases have been postmortem findings. In one of Sanes and Doroshow's cases the patient, a child, was cystoscoped one week prior to death without any gas-containing vesicles being observed; but whether or not the cysts had been present antemortem in the remainder of the cases is unknown. Almost all the cases were associated with a gas-producing colon bacillus infection. Most observers agree that a high blood sugar predisposes the patient to this type of bladder infection. In more than half of the reported cases there had been diabetes, or glucose in saline had been administered by clysis. A number of observers believe that the increased glucose in the urine and bladder tissues may be an etiological factor.

(6) *Pseudomembranous cystitis* may be diffuse or involve circumscribed areas of the bladder wall. It is commonly limited to the trigone (*pseudomembranous trigonitis*). The mucosa is covered by confluent exudates (composed of fibrin, debris, pus, and microorganisms) which form a thin, loosely adherent, grayish or pinkish pseudomembrane, with ragged, detached edges. The adjacent mucosa is usually more or less inflamed. The exudative pseudomembrane is easily freed from the mucosa. The condition may result in ulceration or in gangrenous cystitis.

(7) *Ulceration*, usually superficial, is a common complication of the ordinary forms of chronic cystitis. The ulcers may be single or multiple, and may be located in various parts of the bladder. Vesical ulcers are also seen in connection with specific infections such as tuberculosis, syphilis, typhoid fever, and bilharziasis, or in association with malignant tumors, or chemical or mechanical injury, or following radiation of the bladder, prostate, uterus, or other pelvic organ. These are described elsewhere. The foregoing must be differentiated from localized submucous fibrosis (Hunner's ulcer), which is a separate entity (see Plate II).

Symptoms of Cystitis. Frequency of urination is the most constant symptom of acute cystitis. The onset is usually insidious, but the condition may rapidly become worse, and the frequency is then usually accompanied by dysuria and urgency. The patient may be required to empty the bladder every 15 or 20 minutes during the day and night. The symptoms may become so aggravated in certain cases that there is a constant desire to urinate.

Pain may be felt in the *perineal* or *suprapubic* region. In the presence of retention of urine, there may be more or less steady pain over the bladder.

Hematuria, particularly at the end of urination, may occur in severe cases.

Pyuria is a constant symptom, and may be macroscopically perceptible even to the patient. The urine may be only faintly cloudy, or it may be turbid, and all the receptacles—whether one, two, or even more are used—heavily clouded with blood, epithelial cells, and organisms.

The symptoms of *chronic cystitis* resemble those of the acute process, but are much milder and less pronounced. The desire to void occurs usually every two or three hours during the day and two or three times during the night.

Cystitis does not, as a rule, produce fever, chills, or gastrointestinal symptoms unless there are associated renal or other extravescical diseases, such as pyelitis, pyelonephritis, pericystitis, or prostatoseminal vesiculitis.

Diagnosis. The diagnosis of cystitis is usually determined by the history, physical examination, microscopic examination of the urine, and, in chronic cases, by the appearance of the bladder through the cystoscope. A patient with acute cystitis should not be cystoscoped if it can possibly be avoided.

Obtaining a good history is of the greatest importance, since a patient with symptoms of cystitis may be suffering from a lesion in some remote or adjacent part of the body of which the bladder symptoms may be only one expression. If the patient gives a history of recurring attacks of cystitis, it is probable that some underlying factor—frequently pyelitis or infected hydronephrosis—is responsible for the recurring attacks, the discovery of which is of paramount importance. Of particular significance is a history of tuberculosis, gastrointestinal disturbances or lesions of the rectum or anus, a surgical operation just before the onset of the bladder symptoms, or disease of the female internal genitalia.

For the same reason, a careful physical examination is essential.

Careful microscopic and bacteriological examination of clean, fresh specimens of urine is of the greatest importance in both acute and chronic cases. The urine should be examined as expeditiously as possible. In females, urinary specimens should always be collected by catheter. In males, they should be collected by the three-glass method (100 cc. each), the contents of the second glass being the true bladder urine. The meatus should be carefully cleansed prior to voiding in the sterile container.

An acute cystitis usually subsides within a period of 10 to 12 days unless there is a continuous flow of organisms into the bladder, a traumatic focus causing mechanical irritation, or lesions of the spinal cord, urethra, or bladder neck, preventing complete evacuation of the urine. If the bladder inflammation does not yield to adequate treatment in this time, it should be tentatively regarded as a secondary manifestation of a condition, within or without the bladder, which must be eliminated before a cure of the cystitis can be hoped for. All such patients should have cystoscopic examination.

If the cystoscopic examination reveals a negative bladder, vesical neck, and urethra, then the upper urinary tract must be investigated by means of ureteral catheterization, with examination of separate specimens of urine, and determination of the function of each kidney. If deemed necessary, pyelography or excretion urography should be done. Many cases of chronic cystitis are secondary to infections of the upper urinary tract, which must be eradicated before response to treatment of the bladder involvement can be looked for.

Differential Diagnosis. As the chief symptoms of cystitis—frequency, pain, and pyuria—are also symptoms associated with other inflammatory lesions of the genito-urinary tract, careful interpretation of the findings is essential.

The type of cystitis present is determined by microscopic and bacteriological examination of the urine and, in chronic cases, by cystoscopic examination. The colon bacillus, the chief offending organism in vesical inflammations, is not only readily identified, but the particular strain of colon bacillus may be determined. Granulations, cysts, ulcerations, encrustations, and other inflammatory changes that may accompany chronic cystitis are all recognized by their cystoscopic appearance.

In the absence of bacteria, in women who are going through the menopause, the vesical irritation may be of a non-bacterial type which occurs during this period and which is benefited by the injection of ovarian extract.

Prognosis. Acute cystitis usually clears up promptly under proper treatment unless there is a constant influx of infectious organisms or some obstruction to free urinary drainage. Even the most stubborn of chronic cases will usually yield to treatment, if the general principles of elimination of the source of irritation, removal of any obstruction to urination, and proper treatment of the bladder condition, by general and local measures and oral medication, are observed. Certain cases may,

however, prove very unyielding, requiring prolonged and varied treatment.

Treatment. The treatment of a patient with cystitis involves (1) the relief of the subjective symptoms and (2) the cure of the infection or other underlying cause. In the past, the patient has frequently been recorded as cured once the symptoms had subsided; but modern medicine regards the patient as cured only when the urine is free of pus and sterile on culture. The general principles involved in the treatment of cystitis are (1) elimination of the source of irritation, (2) removal of any existing obstruction to free evacuation of the urine, (3) treatment of the local condition.

It is useless to treat cystitis, with the hope of a cure, without removing the cause, whether it be an infection in the upper or lower urogenital tract or in an adjacent organ, an extravescical mass, a calculus, foreign body, or tumor within the bladder, an obstructive lesion of the urethra or vesical neck, or a systemic condition.

The securing of good drainage of the urinary tract is of primary importance, because any stasis of urine will result in rapid multiplication of the infective organism. Irrespective of the efficiency of the urinary antiseptic employed, a sterile urine will not be obtained if a residual persists. Central nervous lesions may require permanent suprapubic drainage, with vesical irrigations through the tube.

It is important to know precisely what organism or combination of organisms is responsible for the bladder inflammation. Though the colon bacillus is at fault more often than any other, there is a host of less prevalent organisms that cause serious bladder disturbance. The treatment—chemotherapeutic, dietetic or otherwise—will vary in accordance with the nature of the infection, and will therefore be governed largely by the laboratory findings.

Acute Cystitis. During the acute stage, it is important that the patient have complete rest in bed. Hot applications to the suprapubic and perineal regions, and hot rectal or vaginal irrigations, give great relief. Pain is relieved by rectal suppositories of $\frac{1}{4}$ grain of opium and $\frac{1}{4}$ grain of extract of belladonna, or by sedatives administered orally.

The bowels should be kept regulated by means of mild laxatives. urging is always contraindicated. When stasis of the colon contents is allowed to persist, a constant supply of colon bacilli enters the urinary stream through the kidneys, being either blood-borne or conveyed through the lymphatic system.

Cystitis is usually aided by the dilution of the urine by the free drinking of water; but in cases with distressing dysuria, large volumes of fluid will increase the irritation.

Alkalinization of the urine is frequently important in relieving the distressing dysuria of acute cystitis. To this end, a high alkaline ash diet (p. 1192) is prescribed and, in addition, sodium bicarbonate, potassium citrate, or one of the alkaline mineral waters. There are many excellent waters on the market, but in our experience none has proved more efficacious than our own American Kalak water, which is more palatable and has a higher alkaline content than many of the foreign waters.

Tincture of hyoscyamus is an excellent drug for irritable bladders. In severe cystitis from any cause, the following prescription (Kirwin's Mixture) is very helpful:

Potassium citrate	Dr. 6 (24 cc.)
Tinct. Hyoscyami	Oz. 1 (30 cc.)
Tinct. Opil camphorata	Oz. 1 (30 cc.)
Elix. Saw palmetto et Santalwood q s. ad	Oz. 4 (120 cc.)

Sig.:—Dr. 2 (8 cc.) q. 4 hrs.

In less severe cases the following prescription is useful:

Tinct Hyoscyami	Oz. 1 (30 cc.)
Potassium citrate	Oz. 1 (30 cc.)
Aqua ad	Oz. 6 (180 cc.)

Sig :—Dr. 1 or 2 (4 or 8 cc.) q. 4 hrs. in water

Local treatment, such as instillations and irrigations, are not, generally speaking, used during the acute stage. However, the instillation and retention of 1 or 2 ounces of novocaine borate, 2 per cent, will give temporary relief in very acute cases.

Sulfonamide therapy is very useful in acute cystitis of bacterial origin. When other urinary antiseptics are used (methenamine, mandelic acid) most urologists prefer to keep the patient on an alkaline regime for several days to relieve the most distressing symptoms, then administer the antiseptic.

Chronic Cystitis. GENERAL MEASURES. The most important step in the cure of chronic cystitis is the removal of the primary condition (renal, urethral, systemic, etc.) responsible for the cystitis. A person suffering from cystitis should lead a very quiet, non-athletic life temporarily, and should particularly avoid exposure to cold or damp. In

the more severe chronic cases the patient should be confined to the house in cold, wintry weather or sent to a temperate climate.

In general, in cases with dysuria, the patient should be put on a low-protein, alcohol-free diet. All rich foods, condiments, spices, and other irritating substances, such as berries of all kinds, tomatoes, and carrots, should be avoided. Certain forms of infection call for specific diets which will reinforce the effects of the therapeutic measures that are being applied, and these will, of course, vary in accordance with the nature of the infection and the kind of treatment that is being employed to combat it (Diet, p. 1187).

LOCAL TREATMENT. In subacute and chronic cystitis, bladder irrigations have been found very helpful for cleansing the bladder and relieving the pain and congestion (Bladder Irrigations and Instillations, p. 1158). These should be given daily at first, and then two or three times a week. The antiseptic solutions in most common usage are normal saline solution, boric acid, 2 per cent; rivanol dextrose, 1:8,000; acriflavine, 1:8,000; potassium permanganate, 1:8,000. For vesical hemorrhage, silver nitrate, 1:10,000 is useful (but should never be used in vesical tuberculosis). Sodium citrate, 1:8,000 will prevent the formation of large clots.

Granulations and ulcerations may require fulguration.

In very severe cases of chronic cystitis a suprapubic cystostomy is frequently advisable to prevent gangrene. Such cases usually present a severe urosepsis.

URINARY ANTISEPTICS: ACIDIFYING DRUGS AND DIETS. For the active combating of vesical infections, many urinary antiseptics for oral administration have been recommended, none of which is ideal though many have proved merit. Some urologists recommend the use of a urinary antiseptic in the acute stage of a cystitis, while others prefer first to relieve the patient's acute symptoms by alkalinizing the urine. In chronic cystitis, the urinary antiseptics are used as soon as the diagnosis is made, unless there are severe subjective symptoms.

The sulfonamide drugs (sulfadiazine and sulfathiazole in particular) have to a great extent supplanted the older urinary antiseptics in vesical as in other urinary-tract infections.

Methenamine (hexamethylenamine, urotropin) is an efficient and practical drug for the treatment of bacillary infections of the bladder (except tuberculosis) and of staphylococcal cystitis. Since methenamine acts only in an acid urine, an acidifying drug is essential. Methenamine and

acid sodium phosphate, or other acidifying drug, should be given in 4-gram (60-grain) doses during the 24 hours.

Mandelic acid is often effective in infections due to the colon bacillus (*Escherichia*). The urine must be kept below a pH of 5.3 for bactericidal action. Twelve grams of mandelic acid daily, in divided doses, is the usual amount prescribed. The fluid intake is limited to 6 glasses of water in the 24 hours, to insure the necessary urinary concentration of the mandelic acid. If administered in the form of ammonium mandelate, as is commonly done, a secondary acidifying drug is not, as a rule, necessary. When sodium mandelate is used, ammonium chloride (4 Gm.) or other secondary acidifying drug, is required.

It is advisable to combine both methenamine and mandelic acid therapy with a high acid ash diet. The ketogenic diet has been highly recommended for the treatment of colon bacillus infection and other bacillurias in which it is essential to secure an acid reaction of the urine. While it has proved very efficient in some cases, hospitalization is generally necessary for its successful carrying out, and it is unpleasant and upsetting to the patient. The high acid ash diet, reinforced by the oral administration of acid sodium phosphate, sodium benzoate, ammonium chloride or nitrate, calcium chloride, or nitrohydrochloric acid as recommended by Crance and Maloney, is, we feel, a more practical and equally effective method of securing acidity of the urine because it can be carried out at home and is not upsetting to the patient. A valuable adjunct is Poland water, which is neutral and more palatable than distilled water. All ordinary tap water is distinctly alkaline.

Other urinary antiseptics that have been recommended for bladder infections are acriflavine and methylene blue, both of which have a limited usefulness but are irritating to the digestive tract. Pyridium (0.1 Gm. 3 times a day) is helpful when the urine is persistently alkaline.

The above-mentioned drugs and diets are discussed at greater length under *Urinary Antiseptics* (p. 1162); *Nitrohydrochloric Acid in the Treatment of Colon Bacillus Infections* (p. 1186); *Diet* (p. 1187).

Gangrenous Cystitis

Cystitis gangrenosa (diphtheric, exfoliative, or croupous cystitis, cystitis gangrenosa dissecans, necrosis of the bladder) is a superficial or deep necrosis occurring, usually, as a terminal phase of a severe cystitis in greatly debilitated subjects, or as the result of trauma and infection which have interfered with the blood supply of the bladder wall. Stirling

and Hopkins were able to collect 207 cases from the literature up to 1933, and numerous additional cases have since been reported. The condition is probably much more common than is indicated by the published reports, and in every case of severe chronic cystitis the possibility of gangrene should be kept in mind. Many of the recorded cases escaped detection during the course of a profound illness, and were diagnosed only at autopsy.

Etiology. Gangrene of the bladder was once regarded as an excessively rare condition seen almost exclusively in postpartum cases. Several etiological factors are now known to contribute to its incidence: a severe cystitis which has interfered with the blood supply of the bladder wall, or a general infection such as typhoid, diphtheria, or meningitis; trophic disturbances; trauma due to extravascular pressure (uterine displacement in pregnancy, pelvic tumors, prolonged labor, etc.), interfering with the nutrition of the vesical wall; injury from injected chemicals or from x-ray or radium therapy; circulatory obstruction due to the ligation of adjacent arteries, thrombosis, or embolism; and central nervous lesions resulting in urinary retention. Retention of urine, infection, and interference with the blood supply are the chief predisposing causes.

A new etiological factor in the production of vesical gangrene, that has come to the forefront in recent years, is transurethral prostatic resection. A few such cases have been reported, and numerous others have probably occurred without seeing the publicity of print.

Pathology. Any or all of the layers of the bladder wall may be involved in the destructive process. If cystoscopy is possible, there may be made out areas of beginning necrosis, with intense congestion of the trigone and many hemorrhagic areas. The entire wall may be involved in the necrosis, so that it has a dirty, grayish, shaggy aspect. The vesical orifices are usually gaping.

Later, the mucosa loses its histological structure, and may exfoliate off *en masse* or be cast off in small particles as the disease progresses. After separation of the slough, the bladder presents its inflamed musculature, if the involvement has been deep. With subsidence of the acute process, provided the patient survives, regeneration and fibrosis take place, with contracture of the bladder and reduction of its capacity. If much tissue has been lost in the region of the trigone or vesical neck, there may be interference with the ureteral orifices or with the function of the internal vesical sphincter. If the necrosis has been due to inter-

ference with the blood supply to the bladder wall, nature may re-establish nutrition by means of the collateral circulation. The regenerative powers of the bladder epithelium are very great, and not infrequently there is a return to a semblance of normal conditions.

Symptoms and Diagnosis. Of diagnostic importance are the history, urinary findings, cystoscopic appearance of the bladder, and microscopic examination of the exfoliated tissue.

The symptoms are those of a urosepsis. The urine is foul, ammoniacal, and loaded with pus, blood cells, and debris of the bladder mucosa. Bacteriological examination will show streptococci or *Staphylococcus pyogenes* and colon bacilli, with, less often, *S. viridans*, *B. typhosis*, or *B. proteus*. Hematuria is sometimes very profuse. Perforation of the bladder wall and peritonitis may occur. Intermittent occlusion of the catheter, due to plugging with particles of exfoliated tissue, and inability to empty the bladder by catheter, are pathognomonic. Exfoliation occurs late in the disease, however, and the outlook is distinctly poor if the condition is not recognized until it has reached this advanced stage.

Vesical neoplasm and pseudomembranous cystitis must be ruled out. In the latter, the symptoms are usually much less severe.

Prognosis. The prognosis depends upon the severity of the infection and on the degree of necrosis that has taken place by the time treatment is instituted. Gangrenous cystitis is invariably fatal when it occurs as a terminal phase in patients with debilitating disease. If the necrosis has been due to interference with the blood supply to the bladder wall during the course of an operation or a difficult labor, and if the patient's condition was good prior to the operation, the chances of his surviving gangrene of the bladder are good.

Treatment. Early diagnosis is very important, since hope of recovery lies in the prompt removal of the necrosed tissue and the institution of free drainage. This is usually best accomplished by suprapubic cystostomy, although, in women, the greater width of the urethra makes evacuation of the debris easier than is the case with men. As the patient is almost always profoundly septic, even before peritonitis sets in, supportive measures are required to enable him to withstand the infection. Urinary antiseptics should be freely administered by mouth, the bladder irrigated through the cystostomy opening, using the surgeon's preferred antiseptic, and such aids as blood transfusion and subcutaneous infusion utilized if necessary.

Alkaline Encrusted Cystitis

An extremely stubborn form of chronic cystitis quite frequently seen in women, particularly after childbirth, is alkaline encrusted cystitis (chronic alkaline phosphatic cystitis, calcareous cystitis). Its occurrence in men is much less common. The disease is characterized by the appearance of whitish encrustations on the inflamed vesical mucosa or the surface of ulcers or tumors, and by the passage of gritty material in the urine.

Etiology. The cause of these vesical deposits is not definitely established. Experimental work has shown, however, that the lesion is probably due to invasion of an already injured bladder by an organism—usually the *Salmonella ammoniae*—which has the ability to convert urea into ammonia, thereby causing an alkaline reaction of the urine. In this alkaline medium the inorganic salts of calcium, magnesium, and ammonium phosphate are precipitated. The crystals may be implanted on any type of lesion: ulcerous, tuberculous, calculous, malignant, traumatic. Encrusted cystitis may follow an acute cystitis, but rarely does. The usual precursors are chronic cystitis, ulceration, tumor, calculus, urinary stasis due to obstruction, or vesical trauma incident to childbirth or pelvic operations in the female.

Patients frequently give a history of previous fulguration. In this regard, Randall and Campbell have recently suggested that, since salts do not attach themselves to living cells, and their deposition is enhanced by dead cells or fibrin, it may well be that the dead cells caused by electric destruction supply the necessary seed for the precipitation and encrustation of salts from the already alkaline urine—thus explaining the cause for encrustation in some patients with an alkaline urine and not in others.

The *Salmonella ammoniae*, isolated by Hager and Magath, seems to be the organism chiefly productive of this lesion, but other organisms—particularly streptococci and colon bacilli—have been found in these cases by various investigators.

Pathology. The lesions may affect only a small portion of the bladder surface, occurring usually about the trigone and ureteral orifices, or they may be generalized and cover the entire mucous membrane. Flat lesions, resembling a whitish membrane, are sometimes seen; but the more typical lesion is a whitish elevation of crystalline deposits attached to an ulcerated base. The lesion may involve only the mucosa, or the

ulceration and crystalline deposits may extend into the submucosa and even into the muscularis.

Symptoms. The symptoms are those of ordinary cystitis, with, in addition, the passage of gritty material in the urine. In addition to the gritty deposits, the urine contains blood, mucus, and sometimes pus, and is usually strongly alkaline. A peculiarity of the urine, which serves to differentiate this type of bladder inflammation from the commoner forms, is the large number of red blood cells and the relatively few pus cells. General symptoms are lacking.

Diagnosis. The diagnosis is based upon the history, examination of the urine, and the cystoscopic picture.

A history of frequency, dysuria, and the regular passage of gritty material, with a constantly alkaline urine, is pathognomonic of alkaline encrusted cystitis.

Cystoscopically, the bladder presents patches of whitish encrustations firmly embedded in the mucous membrane or adhering to the surface of the underlying ulcer. The affected areas may be few and confined to the trigone or about the ureteral orifices, or the entire mucosa may appear to be covered with the crystalline deposits. When seen in patients of cancer age, these elevated, tumor-like lesions may be taken for malignant neoplasms. Because of the intolerance of these patients to instrumentation, spinal or sacral anesthesia may be necessary.

Treatment. The treatment of these cases is admittedly unsatisfactory, as this form of cystitis is rarely benefited by the methods effective in ordinary forms of bladder inflammation.

Successful results have been achieved in some cases by the introduction into the bladder of the *Bacillus bulgaricus*, followed by injections of mercuric chloride, 1:20,000. This produces an acidity which destroys the alkalinizing bacilli, and when this has been accomplished, the original bladder lesion can usually be treated with some hope of success. The lactic acid bacillus is also used to acidify the bladder contents.

Redewill has achieved considerable success by treatment with a combination of parathyroid extract and a vitamin-A régime.

Recently, good results have been achieved in some cases by the use of the sulfonamides.

In extensive encrustations or rebellious cases, encouraging results have occasionally been obtained by cystostomy with continuous bladder irrigation with a 1 per cent solution of acetic acid through the suprapubic tube.

Surgical measures are curettage, through the female urethra or through a cystotomy incision, and fulguration.

Local measures are of little permanent value, however, if there is a renal infection to rekindle the cystitis. An alkaline upper urinary tract, without infection, will also frustrate local therapeutic endeavors. To obtain a permanent cure in the more chronic and severe infections, with a highly alkaline urine, Randall and Campbell stress the importance of acidifying the entire urinary tract, regardless of the causative organism. Acidification of the urinary tract cannot be obtained by the oral administration of acidifying drugs or by acid-producing diets in the presence of an alkaline encrusted cystitis. Supplementary irrigations of the bladder and renal pelves with acid solutions are necessary to secure an acid reaction, which may then be maintained by acidifying drugs. These authors have found phosphoric acid superior to acetic, lactic, and hydrochloric acids for producing an acid medium. They recommend a 1 per cent solution for the bladder and a 2 per cent solution for the renal pelves. The renal pelves tolerate this solution well, but the bladder may at first rebel, in which case weaker acids, such as citric or acetic acid, are used to build up the tolerance of the bladder until solutions of phosphoric acid up to 1 per cent are accepted. Ureteral catheterization is performed as soon as possible, and in the presence of an infected renal pelvis, or an alkaline urine, intermittent irrigations of the renal pelvis, with a 1 or 2 per cent solution of phosphoric acid, are given. A severely infected pelvis is usually treated through an indwelling ureteral catheter with frequent irrigations for 24 hours or more. Randall and Campbell report excellent results by this method in the most stubborn cases, but warn that at times prolonged and repeated therapy is necessary to obtain a permanent cure.

We have had good results with the use of the following solution for irrigating the renal pelves and the bladder:

Magnesium oxide anhydrous	6.54 Gm.
Citric acid 1. H ₂ O.	32.35 Gm.
Distilled water to make	1,000 cc.

Boil the solution 1 hour, then cool; boil another hour, then cool and make up to 1,000 cc. with sterile distilled water.

Localized Submucous Fibrosis (Hunner's Ulcer)

A bladder lesion of fairly frequent occurrence, especially in women, is localized submucous fibrosis—the “clusive” ulcer described by Hunner

in 1914 and so called because of the proneness of the symptoms and cystoscopic evidence of the ulcer to disappear and then recur. The lesion has been described under many other names—interstitial cystitis, pan-mural ulcerative cystitis, cystitis parenchymatosa, Hunner's ulcer, submucous ulcer, and paracystitis.

Localized submucous fibrosis is a chronic inflammation of all layers of the bladder wall, characterized by hyperemia with minute superficial ulcerations of the mucosa and extensive edematous thickening, particularly of the submucosa. Cystoscopy, however, may reveal only a small abrasion upon the surface of the mucosa, usually in the free portion of the bladder, where it may easily be overlooked. The points of ulceration may be single or multiple. They bleed readily and, when touched, will be found to be exquisitely sensitive. With healing, there is the formation of a fibrous atrophic scar. The lesion is characterized by very troublesome symptoms, absence of striking pathological urinary findings, and the presence of an "elusive" ulcer in the bladder.

The condition is 3 to 4 times as common in women as in men.

Etiology. The etiology is still obscure. Hunner attributed the lesion to a previous tonsillitis or other focal infection, which may have occurred a considerable time before the appearance of the bladder symptoms. Many others also believe it to be due to invasion of bacteria from distant foci. The toxin theory, however, does not explain all cases; nor does it explain the predominance of the disease in women. Some observers believe the fibrosis to be the outcome of a preceding acute cystitis or cystopyelitis, diseases which are more common in women than in men. A high percentage of patients give a history of cystitis or pyelitis, but many others do not. The vesical lesion is frequently associated with granular urethritis, but this is by no means always the case. Hunner found ureteral stricture in one half of 102 patients, and believed this to be a factor. Specimens removed with a cystoscopic rongeur often prove to be negative on bacteriological cultivation, and in most cases the urine is microscopically and culturally negative. The relation of infection to the lesion is, therefore, still problematical.

Other authors think it may be an embolic process.

Fister has recently pointed out the striking similarity between the etiology, pathology, and symptomatology of submucous fibrosis and lupus erythematosus.

In some cases, at least, there appears to be a relationship between the ulcers and the glands of internal secretion. The symptoms are aug-

mented just prior to or during menstruation, and appear to be most severe in those who are undergoing changes due to a natural or artificial menopause.

Pathology. The lesion has the characteristics of a chronic inflammation. Grossly, the involved area of the bladder wall is thickened with edema. The thickening is most marked in the submucosa, but may extend to the paravesical tissue and peritoneal reflection. In the center of the thickened area is a minute ulcer. The thickening is entirely out of proportion to the size of the ulcer or ulcers.

Microscopically, the most extensive changes are those in the submucosa, although all three layers of the bladder wall, and even the paravesical tissues, may be involved. The lesions in the mucous membrane are secondary to those in the submucosa.

Areas resected in early cases show a flattened, thinned-out epithelium, dilatation of the capillaries and lymphatics, and areas of fibrosis and round-cell infiltration in the submucosa. Round-cell infiltration is occasionally seen between the muscle bundles. There is loosening of the intermuscular tissue due to the edema.

The ulcer-bearing area shows a loss of the epithelium. The ulceration may be so superficial that the basement membrane is unimpaired. Occasionally, the surface of the ulcer and surrounding mucosa are covered with fibrin containing many red blood cells.

In the later stages there is proliferation of the submucosal connective tissue, resulting in contraction of the vesical wall and scar-formation.

Symptoms. Localized submucous fibrosis is essentially a chronic disease. Most of the patients, when first seen, give a history of long duration of symptoms.

The characteristic symptoms are pain on distention of the bladder and frequency of urination, with clear, usually sterile urine, and marked *decrease of the bladder capacity*. The symptoms are gradual in onset and intermittent at first, later becoming more constant.

Pain is always the most obtrusive symptom. The pain, which is knife-like or stabbing, and frequently excruciating on accumulation of even 1 or 2 ounces of urine, is aggravated by walking or any undue movement, and sometimes even by intestinal peristalsis. The pain frequently takes the form of distressing pressure. It is usually suprapubic, but may be referred to the rectum, urethra, pelvis, perineum, or inguinal region on the side corresponding to the location of the ulcer.

Frequency of urination varies greatly in severity and from time to

time. It is as great at night as during the day, and in advance cases urination occurs every few minutes, so that the patient is almost incontinent and frequently becomes a nervous wreck. Many women complain that the frequency is more pronounced just before or during menstruation.

The urine, in uncomplicated cases, is macroscopically clear and sparkling. Microscopically, it may show a few leukocytes and red blood cells. At the next examination, however, these may be absent, for the ulcer frequently heals over temporarily and will then give no evidence of its existence detectible by urinalysis. Occasionally our cultures have shown *Bacillus coli communis*, *B. diphtheriae*, staphylococci, and, once, *Streptococcus hemolyticus*, but in the great majority of cases the cultures are sterile.

Intermittent hematuria is a fairly constant feature. It may be gross, varying from very slight amounts to the passage of bloody urine with clots, but more often it is microscopic in amount.

Other fairly common symptoms are burning on urination, difficult urination, terminal strangury, backache, loss of weight, and extreme nervousness.

The severity of the symptoms varies greatly from time to time, and temporary spontaneous relief from symptoms may occur. It is characteristic of these patients that they have consulted many physicians and have been subjected to many types of treatment—operative and otherwise—without relief or with only temporary benefit.

Diagnosis. Localized submucous fibrosis is essentially a disease of adult life, and may occur at any period after youth. It is much more common in women than in men. The marital status appears to be a negligible factor.

The diagnosis is made on the history, urinary findings, and cystoscopic appearance of the bladder.

The symptomatic picture is frequently so characteristic that the diagnosis can almost be made from it alone. A history of pain which is increased on distention of the bladder, marked frequency day and night and gradually decreasing capacity of the bladder, and frequent hematuria on distention, associated with complete or almost complete absence of pus in the urine and negative cultures, should always make one suspect localized submucous fibrosis.

Cystoscopy should always be done, however, and frequent cystoscopic examinations may be necessary before the diagnosis is established.

The introduction of the cystoscope is extremely painful and may necessitate the use of spinal or sacral anesthesia. The vesical capacity is greatly diminished. The lesions are almost always in the mobile portion of the bladder, usually on the posterior or antero-posterior wall.

The cystoscopic picture varies according to the duration of the lesion and the presence or absence of associated urinary-tract infection. Usually, definite ulceration is seen. Sometimes all that can be perceived is a small abrasion of the mucosa; this, when touched, bleeds very easily, or it may be bleeding when it first comes within the range of vision. The usual cystoscopic finding is a circumscribed bright red area, varying in size from a few millimeters to 4 or 5 cm., which stands out in sharp contrast to the normal mucosa. There is marked prominence of the adjacent vessels, with capillary dilatations. These areas may be single or multiple. If multiple, they may be widely separated or closely grouped, and may coalesce invisibly by way of the involved submucosa. The mucous membrane covering the affected area may be intact or may present a small superficial-appearing, exquisitely sensitive ulcer, varying in diameter from 2 to 5 mm. Sometimes the ulcer and the surrounding mucosa are covered with mucous or necrotic material. The mucous membrane of the bladder, except in the involved area, is normal. On distention of the bladder, the thinned-out mucous membrane or the ulcerated surface will often crack, producing characteristic irregular bleeding points. The hemorrhage may be so profuse as to interfere with the cystoscopic examination.

Not infrequently, one may see a dead-white fibrotic area with a small congested area in the immediate neighborhood which may begin to ooze blood on being touched.

In more advanced cases there may be broad, irregular areas of inflammation, with generalized edema, hyperemia, and diffuse bleeding. The ulcers are deeper and granulating, and surrounded by irradiating folds of mucosa. In advanced cases, with marked vesical contraction, it may be difficult to differentiate this lesion from more common forms of inflammation and ulceration.

Differential Diagnosis. Tuberculosis, the clinical course of which is quite similar, must be excluded by smears, cultures, guinea-pig inoculations, and urograms. Granular cysto-urethritis in women also gives a somewhat similar picture, but does not cause contraction of the bladder, and nocturia, which is a constant symptom in submucous fibrosis, is absent. The two conditions frequently coexist, however.

Prognosis. The percentage of cures reported by most authors is not

very encouraging. The immediate results of treatment in most cases are good, but recurrences are frequent. Symptoms may be relieved for many months or even for a year, only to recur. It is therefore necessary to follow a large number of cases for long periods in order to obtain an accurate idea of the prognosis. Almost all cases can be greatly improved, and cure is undoubtedly possible in many if treatment is persisted with.

A follow-up of 47 patients by Crenshaw (1934) indicated that the end-results of various types of treatment may be considerably better than generally they are believed to be. This observer found that after 5 to 25 years 34 of these 47 patients were cured or improved, and 13 stationary or worse. Often, he found, a number of years elapsed after treatment, during which little or no treatment was given; at first improvement was slight but then the patients became entirely well. Whether these were spontaneous cures or late results of treatment is an interesting question. Crenshaw found nothing in this series to warrant the assumption that localized submucous fibrosis predisposes to renal disease or greatly influences the general health.

Treatment. The treatment of localized submucous fibrosis is still a debatable question.

Excision, if complete, effects a cure; but unless the entire involved area can be resected, recurrence takes place. Since the extent of the infiltrated area is distinguishable only with the microscope, it is difficult to tell how much tissue to remove. Moreover, because of the markedly reduced size of the bladder, excision is contraindicated in many of these cases. Radical excision of the ulcer, with a margin of healthy tissue, is Hunner's original treatment of this lesion, and was extensively used in the earlier years. Cures were reported in many cases, but in many others recurrences took place, and in recent years this method has been regarded as of questionable value by many urologists. There is still a place for excision, however, in certain of the cases which do not respond to less radical measures, and there is a growing tendency to believe that it should be done oftener in suitable cases.

Of recent years, fulguration has been considered by many urologists to be the method of choice for the treatment of submucous fibrosis, and the one to be tried first. Immediate and complete relief, lasting for variable periods of time, has been obtained in many cases, but the ultimate results as regards cure are not very gratifying. Following fulguration, as with excision, recurrences have been frequent. To be permanently effective, fulguration must be thorough. Deep fulguration

is neither necessary nor desirable, since it causes massive scarring and may result in rupture of the diseased bladder wall. Superficial fulguration should be carried well beyond the limits of the affected area as observed through the cystoscope. Fulguration is painful, and requires anesthetization—preferably spinal or sacral. Several treatments are necessary, and sometimes as many as 10 or 12. The treatment should be repeated every 3 or 4 weeks until the ulcer has completely disappeared. The need of additional fulguration should be governed by cystoscopic inspection rather than by the symptoms.

Exceptionally, in very severe and stubborn cases, transplantation of the ureters is justified.

Resection of the presacral nerve has been tried, but has not proved valuable, and has been largely abandoned.

In cases associated with ureteral stricture, dilatation of the ureter alone has sometimes afforded relief.

Temporary relief from the symptoms is obtained in many cases by topical applications to the ulcer of corrosive substances such as silver nitrate or phenol, or by instillations of silver nitrate. Hydraulic distention of the bladder, under anesthesia, sometimes gives relief, but is only palliative. It always causes some bleeding, and too forcible distention may cause rupture of the bladder. A few authors have reported immediate relief in a high percentage of their cases by the transvesical injection of absolute alcohol directly into and about the ulcers, but sufficient time has not elapsed to determine how lasting are the results of this method.

Any evident foci of infection should be eradicated. General hygienic and tonic treatment of the patient is valuable in these cases. The irritability of the bladder is not, as a rule, greatly relieved by bladder irrigations or by a change in the reaction of the urine.

There is a group of cases which do not respond to any of the above-mentioned methods of treatment. These are the cases associated with artificial or natural menopause. With this group we have had encouraging results with the intramuscular injection of an alcoholic extract of polyglandular tissue (anterior pituitary, gonadal, adrenal). This is administered 2 or 3 times a week, depending upon the response to treatment. Bladder lavage is given daily, using a 1:5,000 solution of rivanol dextrose.

Leukoplakia of the Bladder

In leukoplakia of the bladder there is an epidermoid transformation of the normal mucous membrane, usually in isolated plaques, but in very rare cases involving the entire mucosa. The characteristic dead-white,

lusterless appearance of the lesion, its smooth surface, and sharply defined border make it easily recognizable through the cystoscope.

Vesical leukoplakia is rare (110 cases, Patch, 1929). It occurs more frequently in men than in women (3 to 1).

Etiology. The etiology is unknown, but the lesion is thought to be an accompaniment of long-standing chronic cystitis. Factors that have been emphasized as being possibly etiological are: long-continued infection, irritation due to calculus or foreign bodies, syphilis, tuberculosis, and trophic deficiencies. The occurrence of chronic cystitis with leukoplakia of the bladder is emphasized by all authors. Bladder stone, although found occasionally, appears to be insignificant as a causative factor. No relationship has been established between vesical leukoplakia and syphilis or tuberculosis. Some writers think it a congenital condition, and due to misplaced embryonal rests of the primitive ectoderm, but this is certainly not true in all cases.

Pathology. The pathological process is marked by proliferation and keratinization of the epithelium, which takes on a cornified epidermoid character (Plate II).

Symptoms. The symptoms are not characteristic. Dysuria, frequency, and pyuria are the most common complaints. Frequently the symptoms induced by a coexisting pathological condition in the bladder dominate the clinical picture. Practically all of the organisms found in bladder infections have been recovered from the urines of these patients. The urinary findings are interesting, however, in that patients frequently give a history of having passed "membranes"—large flakes of desquamated mucous membrane.

Diagnosis. The cystoscopic picture is so characteristic that, having once been seen, its recognition is simple. Other proliferative lesions must be differentiated, and the only means of definite diagnosis is by examination of a biopsy specimen removed with the cystoscopic rongeur.

Cystoscopic inspection in most cases shows irregular, dull white plaques with sharply defined borders, surrounded by normal or inflamed and ulcerated mucous membrane. The plaques may be small and few, or, exceptionally, the pathological process may invade practically the entire mucosa. No blood vessels are visible in the diseased areas. Any part of the bladder may be involved, but the base, including the trigone and neck, is the most common site.

The disease may occur at any time of life (one case has been reported in a four-months-old infant) but appears to be most frequent in the third and fourth decades.

Prognosis. The prognosis is poor, particularly if the involvement is extensive, because the lesion is unbenefited by any known form of treatment. There is a popular belief that these lesions tend to degenerate into squamous-cell carcinoma, but the published reports do not bear this out, only a few cases of their actual association having been reported.

Treatment. The treatment of vesical leukoplakia is seldom satisfactory. Surgical excision of the diseased areas is advisable when possible. Since many of these lesions occur on the trigone or about the ureteral orifices, surgery is often inapplicable, however. Good results have been reported in some cases from high-frequency fulguration, the application of well-screened radium, and pure vitamin-A therapy. Vesical irrigations and instillations with various drugs are sometimes beneficial, but only palliative.

Malakoplakia of the Bladder

Malakoplakia of the bladder is a very rare disease, characterized by soft, yellowish-gray patches on the vesical mucosa. It is more common in women than in men. Malakoplakia may also affect the ureters, renal pelves, and renal parenchyma.

Etiology. Little is known of its etiology. The lesion is inflammatory in nature, and is believed by most observers to be a form of chronic cystitis. The resemblance to tuberculous lesions has frequently been remarked. The colon bacillus has also been held responsible.

Pathology. The lesions appear in the bladder as elevated, soft, confluent, yellowish nodules of varying sizes. They are usually surrounded by a hyperemic zone and are often ulcerated. Histologically, the lesion is characterized by the presence of large cells—these-called malakoplakia cells of Hansemann—which are believed to be phagocytes and contain bacteria, leukocytes, and peculiar cell inclusions called Michaelis-Guttman bodies. The latter, which are also free in the tissues, contain iron and calcium. Accumulations of endothelial leukocytes occur and may confuse the observer, so that a bladder tumor may be suspected.

Symptoms. Frequency of urination is the most prominent symptom. Hematuria is occasionally present.

Diagnosis. The diagnosis is based on the finding of the characteristic Michaelis-Guttman bodies on microscopic examination of tissue removed by means of the rongeur.

Prognosis. The prognosis is much more favorable than that of leukoplakia.

Treatment. The treatment consists of frequent bladder irrigations, fulguration of the nodules, or, in accessible lesions, excision.

Gonorrhea of the Bladder

Involvement of the bladder neck and trigone is a common complication of gonococcal posterior urethritis, but a generalized cystitis is rare. The bladder involvement is an extension of the mucosal inflammation of

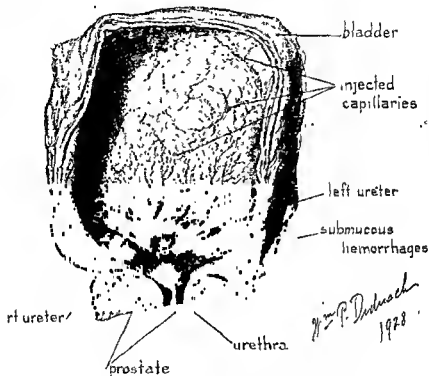


FIG. 225 Acute gonorrheal cystitis. (Christeller.)

the posterior urethra. Subsequently the gonococcal trigonitis or cystitis changes to a mixed infection, staphylococci or other organisms being found with the gonococcus, which prepares the soil upon which these other types of pathogenic organisms find congenial conditions for growth. Chronic infections may take the form of granulations.

Symptoms and Diagnosis. The symptoms are similar to those in other pyogenic infections of the bladder: frequency, with nocturia, dysuria, and pain in the bladder region. All three glasses in the three-glass test will be cloudy and contain pus and organisms.

Treatment. The treatment of the posterior urethritis (p. 717) also takes care of the vesical condition as a rule. Chronic infections may require local treatment, especially if granulations are present.

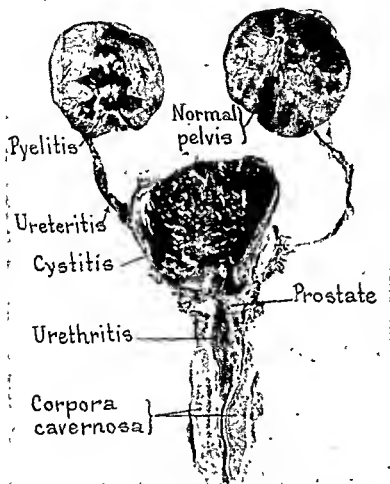


FIG. 226. Gonorrheal urethritis and cystitis. The specimen also shows ureteritis and pyelitis on the right side. (Christeller.)

Syphilis of the Bladder

Syphilis of the bladder manifests itself during the secondary and tertiary stages of the disease. The secondary manifestations, which take the form of macular, papular, and ulcerative lesions coincident with secondary exanthemata of the skin, are very rare. The tertiary lesions, which are always gummatous or papillomatous, are more common. Parasyphilitic affections of the bladder due to lues of the central nervous system are described under *Neurogenic Lesions of the Bladder* (p. 1084).

Incidence. There is no reliable consensus of opinion regarding the incidence of vesical syphilis. Numerous cases of secondary and tertiary luetic lesions have been reported, but in none has the diagnosis been proved by demonstration of the *Spirochaeta pallida*. In most of the reported cases the diagnosis has been based on the presence of vesical lesions and one or more of the following clinical evidences of syphilis: a history of lues, a positive Wassermann reaction, the presence of secondary skin manifestations, response to antisyphilitic medication. Many cases have been diagnosed solely on the basis of therapeutic response. In only a handful of instances have the lesions been subjected to microscopic study.

For many years it was generally believed that the bladder escaped the invasion of syphilis. Authoritative writers (Morris Fournier, Guyon, Nogues, Desnos and Minet, Keyes, Morton) either pass over the subject in silence, or deny the existence of vesical syphilis, or display skepticism regarding the authenticity of the reported cases. Among the earlier writers conceding syphilis of the bladder are Morgagni, who, in 1767, described a postmortem specimen in a subject with undoubted luetic lesions elsewhere, and Follin (1849), Ricord (1851), Virchow (1859), and Vidal de Cassis, all of whom presented cases. Casper, in his *Lehrbuch für Urologie*, states that he has never observed syphilitic ulceration of the bladder, but sees no reason why gummas cannot exist in this viscus. Legueu (1910) and Hallopeau and Fouquet (1911) mention only rare tertiary lesions.

Matzenauer (1900) appears to have been the first to use the cystoscope for the diagnosis of vesical syphilis.

Duroeux, of Paris, in 1913 published the first extensive review of the scattered reports, and collected 26 cases of tertiary vesical syphilis and 14 of secondary lesions, the majority of which had been recorded by French observers. However, prior to the discovery of the Wassermann test and the use of the cystoscope, many cases of vesical lues undoubtedly escaped recognition, so that this paucity of literature is more likely due to failure to recognize the lesion than to actual infrequency of occurrence.

Most of the reported lesions have been tertiary. However, the frequency of mucosal lesions in secondary syphilis would suggest the not uncommon involvement of the bladder mucous membrane at this stage of the infection. If every syphilitic were cystoscoped during the exanthematous stage of the disease, it would undoubtedly be found that the

mucous membrane of the bladder is also commonly involved, even though there are no vesical symptoms.

Pathology. The histopathology of syphilis of the bladder has not been studied very thoroughly. Finestone (1936) found that only 8 of the numerous contributors who have reported cases had subjected the lesions to microscopic study, and, of these, only one case, that of Levy and Tripoli (1933), presented evidence of typical syphilitic histopathology—endarteritis, perivascular lymphocytic infiltration, occasional multinucleated giant cells, and small areas of necrosis. Whether or not the lesions of vesical syphilis present a uniform or distinct syphilitic pathology is still to be determined. Many authors have emphasized the similarity of the papular vesical lesions to condylomata lata.

In not a single reported case has the spirochete been found in either the lesions or in the sedimented urine.

Symptoms. The symptoms are those of any vesical irritation: frequency, dysuria, and sometimes hematuria. The milder secondary lesions are less likely to cause symptoms than the tertiary lesions. However, gummas can exist for long periods without giving symptoms referable to the urinary tract.

Diagnosis. There is nothing characteristic about either the symptoms or the cystoscopic picture of vesical syphilis.

Cystoscopically, the vesical manifestations of syphilis closely resemble lesions much more commonly seen in the bladder, such as hyperemia, simple ulcer, papilloma, tuberculous ulcer, and malignancy.

The hyperemia of the secondary stage of syphilis, however, presents a roseola of the bladder, with scattered, discrete red spots—the so-called macules. Of the several forms which vesical syphilis may take, this is the only one that is pathognomonic. It may be symptomless. The secondary lesions may also take the form of a distinct papular eruption, with or without erosion or ulceration.

The characteristic ulcer is like the specific ulcer on any mucous membrane: more or less elevated on an area of edematous and injected mucosa, the edges sharply defined, projecting, and firm, the base grayish, with necrotic or hemorrhagic debris. The ulcers are usually multiple and clustered, rarely disseminated, and are most often grouped about one or the other of the ureteral orifices (rarely both), where they may readily be mistaken for tuberculous ulcers, particularly if urinary symptoms are present.

In tertiary syphilis the most frequent type of vesical lesion is the

gumma. This is usually ulcerated, but tumefaction without ulceration occasionally occurs. The gummas may be single or multiple. Syphilitic papillomas also occur in the tertiary stage. When viewed through the cystoscope, there is nothing about syphilitic papillomas to differentiate them from benign papillomas. The same difficulty of recognition attends the gumma of tertiary syphilis. It is an infiltrating growth, which may readily be mistaken for a malignant neoplasm.

Most frequently the lesions of vesical syphilis are situated on the trigone, about the ureteral orifices and sphincter.

The diagnosis of vesical syphilis cannot, therefore, be made upon the cystoscopic findings alone. It must be supported by the following corroborative clinical findings: a previous history of lues, evidence of active syphilis elsewhere, a positive Wassermann reaction, response to antiluetic treatment. Microscopic examination of tissue should be done more often.

Prognosis. If the lesion is recognized and treated, the prognosis is uniformly good. A few instances of recurrences have been reported, but these have usually responded to repeated antiluetic treatment.

Treatment. The treatment is that of syphilis in general.

Tuberculosis of the Bladder

Tuberculosis of the bladder is probably always secondary to tuberculosis of the kidneys or seminal tract. In the majority of cases the primary focus is renal. From the patient's point of view, however, the bladder involvement is likely to be of primary importance. The distressing vesical symptoms for relief of which he seeks medical aid are usually of far greater moment to him than the silent, relatively painless process going on in the kidney or in the seminal tract. Vesical involvement is a fairly late complication of a urinary or genital tuberculosis, and cystitis may be present for some time, even in a patient known to have tuberculosis in some organ outside the urogenital tract, before its real significance is appreciated.

Mode of Infection. Involvement of the bladder secondary to a tuberculous focus in the prostate and urethra apparently occurs by direct mucosal extension. In such cases the trigone is practically always the point of first attack. Invasion of the bladder mucosa by continuity from a source in the upper urinary tract also occurs, the first bladder lesions appearing about the ureteral orifice on the side of the affected kidney. In most cases, however, the vesical involvement appears to be due to the

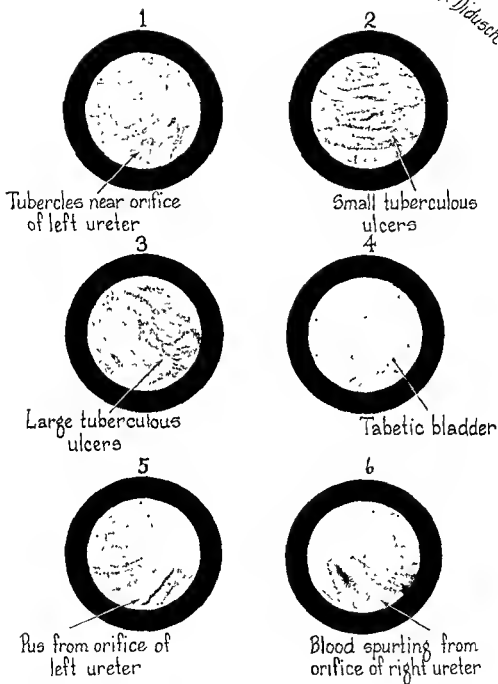


PLATE III VARIOUS PATHOLOGICAL CONDITIONS OF THE BLADDER CYSTOSCOPIC VIEWS
(1, 2, 3) Vesical tuberculous (4) Tabetic bladder (5) Pus issuing from orifice of left
ureter. (6) Blood spurting from right ureteral orifice.

planting of tubercle bacilli from infected urine directly on the vesical mucosa, the resistance of which has been lowered by continuous irritation by urine infected with tubercle bacilli. The earliest lesions are usually in the neighborhood of the ureteral orifice through which the infected urine enters the bladder. Whether or not the vesical infection is ever of hematogenous origin is a moot question.

Pathology. The earliest pathological changes—edema and inflammation of the mucous membrane—are seen about the orifices (Plate III). No bacilli or tubercles are found in these inflammatory areas, and they apparently constitute an early pre-ulceration stage of the inflammation.

As the disease progresses, the lesions extend about the bladder in the form of a diffuse inflammation or, more frequently, as scattered, irregular areas of granulations. Ulceration subsequently ensues, with the development of shallow, irregular ulcers having a hemorrhagic base. The exudate at the base contains many scattered tubercle bacilli. Tubercle-formation is not present at this stage.

A slightly later stage is characterized by lymphocytic infiltration involving both the mucosa and submucosa. The edges of the ulcer are thickened and fibrous. The base is necrotic and invades the muscularis. Tubercles are sometimes found in these later stages. Ultimately the mucosa becomes ulcerated over large areas. Widespread ulceration, with infiltration and fibrosis of the bladder wall, results in marked contraction of the bladder. Pericystitis with adhesions occurs. The ureteral orifices become strictured and infiltration at the vesical neck causes rigidity.

In other cases, tubercles appear in a rapidly progressive tuberculous infiltration of the entire bladder wall.

As a rule, tubercles develop in the bladder only in cases of extended chronicity.

Symptoms. Frequency of urination is the initial symptom, and is often the only symptom over a long period. If no secondary infection has been superimposed upon the tuberculous cystitis, it may be several months before slowly increasing pain on urination and nocturia direct the patient's attention to his bladder. Pain is usually most severe at the end of urination, and, in the later stages, when there is a constant and urgent desire to urinate, is practically continuous and often agonizing.

Slight, intermittent hematuria, imparting a reddish tinge to the urine, may be early in evidence. More profuse hemorrhage following micturition usually implies ulceration of the bladder.

In the later stages, the urine is heavily clouded, due to pus.

Diagnosis. The diagnosis must rest on the demonstration of tubercle bacilli in the urine and the appearance of the bladder through the cystoscope. Guinea-pig inoculation will often serve to clinch the diagnosis.

A history of frequency, urgency, and dysuria, especially if associated with terminal hematuria, is suspicious. The presence of pus and the absence of the common pyogenic organisms by smear is strongly suggestive of tuberculosis, and calls for repeated search for acid-fast bacilli by staining of the urinary sediment, guinea-pig inoculation, and culture. Mixed infections are not uncommon, particularly in the later stages, so that the finding of common pyogenic organisms does not exclude tuberculosis.

Smears, properly stained, will show acid-fast organisms in a high percentage of positive cases. Doubtful cases, and all those in which acid-fast bacilli have been demonstrated, should be further examined by guinea-pig inoculation or culture. The smegma bacillus, commonly found in the male urethra, is also acid-fast. Although requiring more technical skill than the guinea-pig test, cultures are undoubtedly of value, especially when a report is desired in less than the 6 weeks usually required for inoculation.

In suspected cases, repeated examination of the bladder urine is necessary, since pus and organisms vary from day to day.

Cystoscopy, in cases of tuberculosis of the bladder, is often very difficult because of the contracted and supersensitive bladder. Thorough anesthetization is always necessary.

The cystoscopic appearance of the mucous membrane may vary, according to the stage of the process, from a limited inflammatory areola adjacent to one ureter, to an extensive sloughing, ulcerative cystitis in the advanced stages. If secondary to renal involvement, the earliest lesion is usually around the ureteral orifice on the side of the involved kidney, and consists of hyperemia without tubercle-formation. If the infection has existed for some time, tubercles may be in evidence. The tubercles appear as small, yellowish bodies with a hyperemic areola. They ultimately break down and then form irregular, varying-sized ulcers with undermined edges and ragged, dirty, yellowish bases. The ulcers may involve the trigone and the vesical orifice. If the vesical orifice is involved without the ureteral orifices, one immediately suspects that the lesion originated in the seminal tract and extends from the posterior urethra back into the bladder. The lesions may spread so that extensive

areas, including the dome of the bladder, are involved. In extensive ulceration, the entire musculature becomes infiltrated, the infiltration and subsequent fibrosis resulting in marked contraction of the bladder.

In advanced vesical tuberculosis the effect upon the trigone is peculiarly characteristic. If the ulcers are deep and extensive, they will often undermine the edges of the trigone, so that the entire muscular structure stands up from the surrounding wall in a striking manner. The process may even advance so far as to "dissect" the trigone free from the vesical wall except for a frail attachment at the corners.

Occasionally one sees in the same bladder tuberculous lesions in different stages of development.

Although the early lesions are most likely to be seen adjacent to the ureteral orifice expelling infected urine, it should be emphasized that this is not a constant finding. Occasionally areas of inflammation and ulceration are observed distant from the ureteral orifice expelling the infected urine, but with no evidence of inflammation about the orifice.

In badly diseased bladders indigo-carminc is useful in locating invisible ureteral orifices.

Prognosis. If the source of the vesical infection (usually a tuberculous kidney) is removed, the bladder condition often heals rapidly, under the influence of various forms of treatment to be described in detail later. If, on the other hand, the original source of the disease is not eliminated, it is practically impossible to cure or even materially relieve a tuberculous cystitis.

The prognosis, following removal of the source of infection in the upper urinary tract or in the genital tract, depends in a large measure on the degree of vesical involvement. Cases with extensive ulceration, trabeculation, and contraction are the most unfavorable; but it is surprising how often even advanced lesions of the bladder will heal after nephrectomy.

In spite of nephrectomy and continuous postoperative treatment, some bladders refuse to heal. The usual course, in such cases, is damage to the remaining healthy kidney by the effects of back pressure due to contraction about the intramural portion of the ureter, and, ultimately, spread of the disease to the healthy ureter and remaining kidney. The sufferings of these patients may be materially relieved and their lives prolonged in some cases by cutaneous ureterostomy.

Treatment. The ideal treatment of vesical tuberculosis is preventive, namely, early diagnosis and removal of the primary focus in the kidney or genital tract, before bladder involvement occurs. Because of the

frequent absence of symptoms in the earlier stages of renal and genital tuberculosis, such prevention is difficult, if not impossible, of accomplishment.

Treatment of tuberculous cystitis consists in (1) eradication of the focus of infection, usually a tuberculous kidney, if possible, and (2) the placing of the patient upon a hygienic, dietary, physiotherapeutic, and medicinal régime directed to helping him build up resistance against tuberculosis, both generally and locally.

Following nephrectomy, or ureteral occlusion resulting in auto-nephrectomy, or removal of an infectious focus in the genital tract, the tuberculous cystitis, if in the early stages, will often clear up promptly without further treatment other than rest. It has repeatedly been demonstrated that even severe cystitis may quickly heal once the continuous stream of infection has been permanently cut off.

Unfortunately, however, interruption of the bacilli-laden urinary stream from the kidney to the bladder is not always followed immediately by alleviation of the vesical symptoms. The secondary tuberculous lesions in the bladder may be so firmly established before removal of the primary focus that months or even years may be required for a regression of the bladder lesions.

The treatment of patients with continued secondary vesical lesions, as well as those who are unsuited for surgery because of bilateral renal pathology or other adequate reasons, is described in detail under Treatment of Inoperable and Postoperative Urogenital Tuberculosis (p. 1196). Briefly, it consists of rest, fresh air, a special diet, vitamin therapy, tuberculin in selected cases, quartz-light therapy externally and intravesically, bladder instillations and irrigations, fulguration of bladder ulcers, ureteral dilatations, renal-pelvic lavages, and prostatic and seminal vesicular treatments.

Surgical measures for relief of the bladder symptoms are rarely indicated. However, in very severe cases which have failed to yield to any other types of treatment, cutaneous ureterostomy may relieve the symptoms and prolong the patient's life.

Recently, Lazarus and others have found sub-erythema doses of x-ray therapy applied over the bladder definitely useful in alleviating pain.

Bilharziasis

Vesical bilharziasis is due to invasion of the parasite *Schistosoma haematobium*. It is very common in Egypt and other southern Mediter-

anean countries, Arabia, and South Africa. The infrequent cases seen in the United States are acquired in regions where the disease is endemic and imported into this country.

Etiology and Pathogenesis. While there are several varieties of blood flukes closely related to *S. haematobium*, this type (the African blood fluke) has a predilection for the urinary organs and is therefore of special

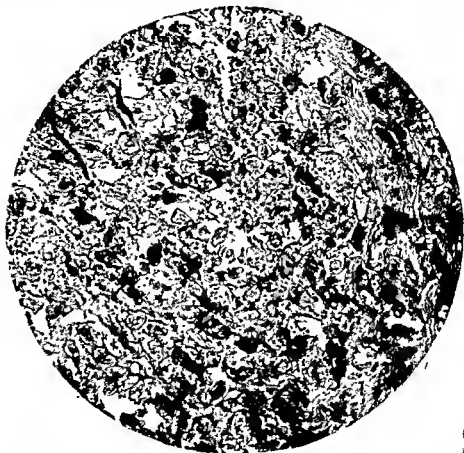


FIG. 227. Bilharziasis of the bladder. Photomicrograph of a cross section of a piece removed from the bladder lesion of a woman suffering from bilharziasis. The ova are packed tightly into the bladder wall.

interest to urologists. Bilharz, in 1851, first identified this parasite with the disease.

Schistosoma are unisexual, flat worms found in pairs, the slender, thread-like, brownish female lying in a groove on the ventral surface of the shorter, broader, whitish male. The mature male is about 15 mm. long, the female about 20 mm.

The larvae (cercariae) are the infective stage of the parasite. They enter the human body through the skin and mucous membranes and mature and mate in the portal vein. Thence the symbiotic pairs migrate to the small veins of the submucosa of the bladder, and may actually live in the pubic, vesical, and uterine plexuses. The eggs are deposited, for the most part, in the base of the bladder and terminal portion of the ureter, where they set up an irritation and produce the characteristic disease. The ova which pass through the mucosa are discharged in the urine. As they work through the tissues into the lumen, they develop a ciliated larva (miracidium). Upon coming into fresh water, the ova release these ciliated larvae, which are not infective to man and die in from 24 to 40 hours unless they can penetrate to the interior of certain species of fresh-water snails, which are found only in certain localities. Having gained admission to the intermediate host, the larvae form sporocysts, which become the cercariae. These leave the snail and move by their flagellated tails toward the surface of the water.

Pathology. The vesical lesion is a chronic granulomatosis, the result of infiltration of the tissues of the bladder wall with the mature worms and their ova and the subsequent tissue reaction.

The lesions are usually limited to the trigone, ureteral orifices, and posterior wall of the bladder, but in far-advanced cases may involve the entire bladder. They most commonly affect the mucosa and submucosa, but may lie in the deeper vesical tissues. The mucosal and submucosal lesions are readily detected by cystoscopic inspection. If the eggs do not penetrate the mucosa, but remain *in situ* and become calcified, a "closed infection" results, with absence of clinical manifestations. Such cases can be diagnosed during life only by the roentgen ray.

Widespread lesions, particularly if they involve the deep tissues, result in fibrosis, calcification, and contracture of the bladder. Urinary fistulas may occur. Obstruction of the ureteral orifices by the papillary granulations, which are usually found in this location, eventually results in renal complications. Detached portions of calcified or encrusted papillary structure frequently act as nuclei for the formation of vesical calculi. Bilharzial carcinoma is not uncommon, and may resemble any of the ordinary forms of vesical carcinoma.

Lesions similar to those in the bladder are commonly found in the ureter, particularly in its lower third, and less often in the renal pelvis, prostate, or seminal vesicle.

Symptoms. Penetration of the skin by the cercariae may be followed

by intense pruritus and erythema, or may go unnoticed. Four or 5 weeks later, toxic symptoms occur: malaise, fever, headache, and cough.

The symptoms of bladder invasion may appear several weeks or months later, or may not manifest themselves for years. Often the urologist is first consulted 8 to 10 years after the original infestation, at which time ova are rarely present in the urine.

Hematuria is the most prominent vesical symptom. It is usually slight in amount and terminal in character, and may be present for a long period without causing the patient any inconvenience or concern. In cases of gross ulceration, however, the bleeding may be profuse. Hematuria does not occur if deep-seated (closed) lesions only are present.

There may be slight urinary frequency and burning on micturition. With secondary infection and encrustation, the urinary distress is greatly increased. Symptoms of obstruction and renal deficiency are frequent in advanced cases.

In most cases the ova are discharged in the urine in great numbers and are easily detected in the centrifuged specimen.

In milder cases, symptoms may be entirely absent. Such a case was that seen by Lowsley. The patient was a Norwegian woman who had lived in East Africa for several years, and had developed the disease but apparently been cured. Ten years after leaving Africa she was instructed to report for cystoscopic observation merely as a check-up of her condition. She presented herself, symptom-free. Cystoscopic examination revealed a congested area about 1.5 cm. in diameter on the right wall of the bladder. This was elevated, slightly granular, but not ulcerated. Microscopic examination of a piece of tissue removed with the rongeur showed it to be completely filled with the ova. She was rapidly cured by intravenous administration of tartar emetic.

Diagnosis. The diagnosis is made by finding the ova in the urine or, as in our case, in the tissue. The ova are ovoidal, slightly narrowed at one end, with a terminal spine attached to the narrow end. Cystoscopy and x-ray examination are important diagnostic aids.

The mucosal and submucosal lesions are easily detected by the cystoscope, and are readily identified by one familiar with the disease. Makar (1932) has given a very complete picture of various types of bilharzial lesions as seen through the cystoscope. The mucosal lesions may appear as one or another of the following: (1) slightly elevated patches of hyperemia, the earliest change detectable by the cystoscope but in no way pathognomonic; (2) bilharzial tubercles—tiny, pale yellow granules

projecting slightly from the mucous membrane, and sometimes surrounded by a zone of hyperemia; (3) bilharzial nodules—grayish nodules that may coalesce to form a bilharzial node, which eventually may ulcerate or become calcified; (4) bilharzial ulcers, which, in uncomplicated cases, are generally small, single, and superficial, but, when due to secondary infection of bilharzial tubercles, may be extensive; (5) bilharzial papillomas—growths of varying sizes that resemble the ordinary vesical papilloma, may be single or multiple, are usually found on the posterior wall or at the ureteral orifices, and frequently contain deposits of calcium salts.

Submucosal infiltration with bilharzial ova produces tumor-like masses, which may be of considerable size and are usually located on the floor and the posterior wall of the bladder. The overlying mucous membrane may be normal or covered with tubercles, nodules, or papillomas. When the infiltration is in the deep vesical tissues only, the extent of the accompanying fibrosis and calcification cannot be studied cystoscopically. The mucosa, however, may be pale, avascular, and present a "ground-glass" appearance. There may be trabeculations, hypertrophy of the wall, and marked contracture of the bladder.

Afifi, in 1930 and again in 1934, called attention to the "cloud-like" shadows and calcified demarcations of the bladder and lower ureter in cases of long-standing bilharzia. The shadows, which are due to depositions of calcified eggs in the mucous, submucous, and muscular layers of the affected organs, he regarded as highly suggestive of the disease, although chronic cystitis from other causes also may produce them. The calcified demarcations are caused by infiltration of the urinary tract by calcified eggs, and often appear in the roentgenogram as shadows of the density of osseous tissue which sometimes outline the bladder, ureter, or urethra. Afifi believed them to be pathognomonic.

Prognosis. The prognosis in early and simple, uncomplicated cases is good. Advanced cases, with fibrosis, contracture, and complications, are serious problems. The parasites do not multiply in the human body, and the extent of the bladder involvement will therefore depend largely upon the severity of the initial infestation, the opportunity for repeated infestations, and the degree of secondary infection. The parasites are, however, long-lived, and may exist as a symbiotic pair in the bladder wall for years.

Treatment. The treatment consists of intravenous injections of tartar emetic. The injections should be given on alternate days over a period

of 15 to 30 days, beginning with $\frac{1}{2}$ grain and increasing by $\frac{1}{2}$ grain until $2\frac{1}{2}$ grains are administered, and continuing thus. Usually a total of 20 or 30 grains is adequate. A newer antimony compound—fouadin— injected intramuscularly, is preferred by some therapists. A 3 per cent solution of emetin hydrochloride is also effective. This is given in $\frac{1}{2}$ to 3-grain doses until 15 to 20 grains have been administered.

These agents will kill the parasite and arrest the disease. Obstructing papillomas and ulcers, however, may require fulguration before the symptoms are relieved. Ureteral, renal, and other complications require appropriate treatment.

Echinococcus (Hydatid) Disease of the Bladder

Echinococcus disease of the urogenital tract is uncommon and is confined chiefly to the kidney (Echinococcus Disease of the Kidney, p. 1520). It is caused by a parasitic tapeworm, the *Taenia echinococcus*, which inhabits the alimentary tract of the dog. Its ova, containing hooked embryos, may invade the intestinal tract of man, whence the embryos occasionally are carried by the blood stream to the kidney. Here they develop into hydatid cysts, which may reach a considerable size. Within the primary or mother cyst are developed many daughter cysts. The daughter cysts or the hooklets may pass down the ureter in the urine. They usually pass out of the bladder but in rare cases may be retained there.

Actinomycosis

Etiology. Actinomycotic infiltration of the bladder wall occasionally occurs. Actinomyces gain entrance to the body, as do other organisms, by being ingested or inhaled, or by direct penetration, usually through a cut or abrasion. The bladder is invaded either by extension from adjacent organs by continuity of tissue or—probably rarely—by a hematogenous process from distant sites.

Pathology. Microscopic examination shows granular tissue with central necrosis and, in the necrotic center, sulphur-yellow bodies consisting of compact masses of the mycelia of the actinomyces (Actinomycosis of the Kidney, p. 1525).

Symptoms and Diagnosis. There may be frequency, burning on urination, and hematuria. Local symptoms are sometimes entirely lacking. The urine shows red blood cells, pus cells, and, occasionally, long filaments. The diagnosis is established by cultural examination of the urine as recommended by Shaw (1933) and by biopsy.

Cystoscopically, the vesical lesions resemble tuberculous ulceration.

Prognosis. The prognosis is poor, since the disease is usually widespread by the time the vesical lesions are diagnosed.

Treatment. The best results seem to have been obtained by the administration of high-voltage x-ray therapy externally and large doses of sodium iodide orally.

Amebic Cystitis

Amebae rarely invade the urinary tract. Ten cases of amebic cystitis were collected from the literature by Franchini in 1928, and 2 cases of *Entameba histolytica* infection of the bladder have since been reported (Van Duzen, 1935; F. D. Thomas, 1936). The amebae are believed to be transmitted to the bladder by the lymphatics or the blood stream from an initial source in the intestinal tract. A few observers believe that they may gain entrance through the urethra.

Symptoms and Diagnosis. The most common symptoms are frequency, dysuria, pyuria, and terminal hematuria. The presence in the urine of *Entamebae histolytica* is diagnostic.

Cystoscopically, a portion of the bladder wall, usually in the trigonal region, will be found congested and covered with vesicular swellings varying in color from a pink to a deep red. The unaffected portion of the wall may be almost normal in appearance or diffusely reddened. There may be considerable hemorrhagic reaction about the cysts.

Treatment. Treatment consists in the administration of emetin, which is specific. Local treatments, including fulguration, are merely palliative (Van Duzen).

Trichomonas Vaginalis Infestation of the Bladder

The *Trichomonas vaginalis* is an infrequent contaminator of the urinary tract. Infestation of the bladder occasionally occurs, however, the organism being an invader from the vagina of the female. As might be expected, it is the female bladder which is most often involved, almost always in association with vaginitis due to the trichomonas. Very few cases of actual bladder infestation in the male have been recorded. A number of cases of trichomonas urethritis in the male have been reported, in most of which the organisms were demonstrated in the urine; but involvement of the bladder was not definitely mentioned. We ourselves have seen the organism in the urine of the male on several occasions.

Symptoms. Invasion of the bladder produces symptoms of cystitis of moderate degree: frequency, urgency, burning, and sometimes hematuria and pyuria. In women, there is almost always an accompanying vaginal discharge and other gynecological symptoms.

Diagnosis. The diagnosis is made by finding the organisms in the centrifuged urine or in the urethral or vaginal secretions.

The appearance of the organism has been described under *Trichomonas Infestation of the Male Urethra* (p. 642).

The cystoscopic picture, while not pathognomonic, is of considerable diagnostic value when taken in conjunction with the history and the findings of urinary and vaginal examination. It has been well described by Heckel, who cystoscopically examined 43 women suffering with *Trichomonas vaginalis* infection of the bladder and urethra. The lesions are usually confined to the trigone and vesical neck. The affected mucous membrane has a fluffy, granular appearance and may sometimes resemble bullous edema. In some cases the mucous membrane appears to be overlaid with a pearly white layer with sharply demarcated borders, surrounded by areas dotted with small, circumscribed, petechial hemorrhages. In other cases, the pearly, granular appearance of the mucosa is limited to the internal urethral orifice, and the chief changes in the bladder can best be described as a "strawberry" trigone, in which the mucous membrane is rough and seedy in appearance and is the site of numerous, small, circumscribed hemorrhages.

Prognosis. The infection clears up rapidly under proper treatment. Recurrences, while frequent, usually respond to repetition of the treatment.

Treatment. Bladder irrigations, faithfully persisted in, are effective in most cases, although recurrence is common, especially if the infecting partner is not under control. Various solutions have been recommended: acriflavine; weak silver nitrate solutions; mercury oxycyanide, 1:4,000; daily irrigations with boric acid solution, followed by the instillation of 15 cc. of mercurochrome solution.

Tumors of the Bladder

Few subjects in urology have received the extended consideration that during the past two decades has been given to vesical neoplasms. The introduction of fulguration (Beer, 1910), improvements in irradiation therapy, and progress in the clinico-pathological classification of bladder tumors have changed our conception of vesical growths and their treat-

ment, and inspired greater efforts toward their control. There is still, however, considerable confusion regarding the pathology, biology, and therapy of bladder tumors.

The vesical neoplasm is a relatively common lesion, and one likely to be encountered by any one engaged in the practice of medicine. It therefore presents a problem in which every medical practitioner should take an active interest, whether he be specializing urologist or family doctor.

Classification and Pathology. The majority of bladder tumors (95 per cent) are of epithelial origin. Sarcoma and the rare benign tumors of mesothelial and heterotopic origin make up the remainder.

Ewing has stated that the natural history of epithelial tumors of the bladder is determined by the structure of its mucosa and the physical conditions to which it is exposed. The transitional character and glandular properties account for the histological varieties of tumors arising from it. Thus, the superficial cells are largely squamous, while the deeper cells rapidly become polygonal, and in many cases deep-lying crypts (Brunn's follicles) are present and show a lining of polygonal or columnar cells. Muscular activity and a constant bathing in fluid account for the villous form of the tumors. Multiplicity may be referred to ready diffusion of the irritants, which cause inflammatory and then neoplastic overgrowth.

Many attempts have been made to classify vesical neoplasms, none of which is satisfactory.

The widely used grading of A. C. Broders, of the Mayo Clinic, is based on the probable *degree of malignancy* of a tumor. If a tumor shows a marked tendency to differentiate—that is, if about 100 to 75 per cent of its structure is differentiated epithelium, and 0 to 25 per cent undifferentiated, it is graded I; if the differentiation ranges from 75 to 50 per cent, and undifferentiation from 25 to 50 per cent, it is graded II; if the differentiation ranges from 50 to 25 per cent, and undifferentiation from 50 to 75 per cent, it is graded III; if there is little or no tendency to differentiation, that is, if differentiation ranges from 25 per cent to practically 0, and undifferentiation from 75 to 100 per cent, it is graded IV. This classification is extensively followed throughout the United States.

In many clinics, however, pathologists and surgeons still prefer the older classification according to the *histopathological structure* of the tumor.

At the Brady Foundation, in the New York Hospital, we more and

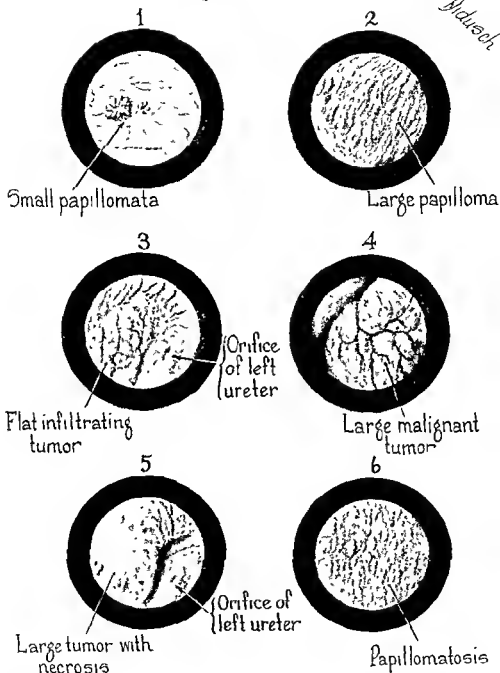


PLATE IV. TUMORS OF THE BLADDER. CYSTOSCOPIC APPEARANCE OF DIFFERENT TYPES OF VESICAL NEOPLASMS

more incline to the belief that while many epithelial tumors of the bladder are undoubtedly benign, *all such tumors are potentially malignant*, and that whatever treatment be elected, we must bear in mind the necessity of providing against such future dangers. Clinically, we group vesical new growths as follows:

1. Papilloma (benign); papillomatosis
2. Papillary carcinoma
3. Non-papillary ("solid") tumors, with infiltration
4. Adenocarcinoma and adenoma
5. Mesoblastic tumors.
 - a. Sarcoma
 - b. Benign growths—fibroma, myoma, myxoma, angioma, etc.

Papilloma; Papillomatosis. Fully 90 per cent of bladder tumors are papillary in character. Some are unquestionably benign, and may remain so for many years; some are malignant from the start; while others become malignant after variable periods. The marked tendency of the so-called benign papilloma to become malignant, and the ill-defined demarcation that exists between benign and malignant growths, have led most urologists and pathologists to regard all vesical papillomas as potentially malignant, even if, initially, they can be proved benign.

Ordinarily the papilloma appears as a pedunculated villous or papillary growth arising from the mucous membrane, having a shaggy surface with out-cropping branches. A papilloma may be sessile, but this type is less frequent. Of the two types, the sessile tumors have a more noticeable limiting membrane about the cells, and the cells show a more active mitosis. Some papillomas have a wart-like and others an almost smooth surface. The size of the growths varies greatly. Some are small and may remain so over long periods. Both the pedunculated and the more malignant sessile tumors may attain considerable size.

Papillary tumors may arise from any portion of the mucosal surface, but are generally found on the trigone or lateral walls, frequently around the ureteral orifices.

In more than half of the cases the papillomas are multiple, and in some instances almost the entire wall is the seat of numerous villous outgrowths. The condition is then termed *papillomatosis*. Histologically, there is no difference between the single and the multiple forms.

Microscopically, the typical simple papilloma shows multiple connective-tissue stalks containing thin-walled blood vessels; these are surrounded by an *orderly arrangement of epithelial cells in one or more*

layers, resembling the vesical epithelium. As a rule, a well-defined basement membrane separates the cells from the core. The epithelial cells, which are attached at right angles to the stalk, range from columnar to transitional, and are more or less uniform in size, shape, and staining

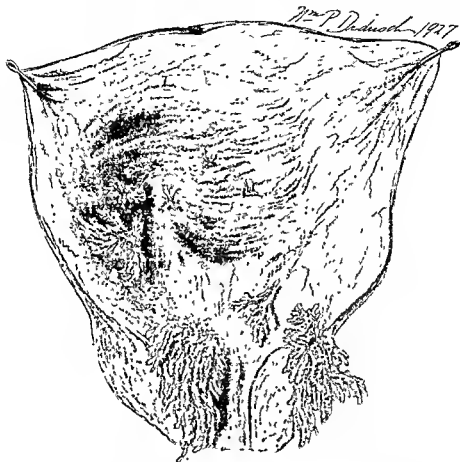


FIG. 228. Multiple papillomas of the bladder involving the vesical orifice, the regions about both ureteral orifices, and the post-trigonal region. (Specimen from the collection of Dr. Legueu, Hôpital Necker, Paris.)

properties. The superficial cells are largely of the squamous type, while the deeper cells are polygonal or columnar. Glandular or cystic formations may be present, or an inflammatory process may cause a leukocytic invasion of the central stalk, but these should not be mistaken for malignancy.

Evidences of malignancy are: variations in the size and shape of the cells, with nuclei staining more deeply and of odd shape; atypical mitoses

in the cells; giant cells; multinucleated cells; fusion of adjacent papillae; loss of orderly arrangement of the cells; breaking through of the basement membrane and infiltration of the stroma.

Where there is no microscopic evidence of malignancy, the tumor is usually classed as "benign." Benign and malignant papillomas may coexist in the same bladder.

From the clinician's standpoint, of more importance than fine distinctions in the grade of malignancy present is the question as to whether or not a tumor has infiltrated the surrounding tissues.

Papillary Carcinoma. Papillary carcinoma is the papilloma with malignant infiltration at the base and in the underlying bladder wall. It is the most common type of vesical carcinoma. It may be polypoid in form, growing into the vesical cavity, or of the infiltrating type characterized by absence of a pedicle, greater infiltration of the bladder wall, and frequent ulceration. In early cases of papillary carcinoma there may be little to differentiate it from the papilloma generally regarded as benign—infiltration being evident only on microscopic examination. In advanced cases, the marked ulceration and infiltration of the wall present a characteristic picture. The extensive necrosis may cause sloughing away of the papillary portion, leaving only the infiltrated base surrounded by a fringe of exuberant tissue.

Microscopically, the picture is that of malignant papilloma with infiltration of the submucosa, musculature, and, sometimes, of the perivesical tissues.

Flat Infiltrating Carcinoma (Squamous Cell). The less common flat, infiltrating type of carcinoma takes the form of a sessile, cornifying epithelium which projects but little into the vesical cavity but progresses laterally and invades the deeper tissues. From the beginning it is deeply and rapidly infiltrating. It is the most malignant of the vesical neoplasms and is radioresistant. Grossly, it appears as a malignant ulcer with hard, everted, advancing borders. *Microscopically*, relatively thick connective tissue is seen between the cell nests, as distinguished from the papillary type of carcinoma. The cells progress along the surface of the bladder while simultaneously they invade the deeper layers of the wall. The clusters of cells are of the squamous type, and become paler in color and larger as the center of the cell nest is approached. At the center, epithelial pearl-formation is usually to be observed, and sometimes prickle cells are also in evidence.

Leukoplakia (p. 1019) is commonly regarded as a precursor of squamous-cell carcinoma.

Adenocarcinoma and Adenoma. Adenocarcinoma primary to the bladder is a rare, highly malignant neoplasm closely resembling adeno-



FIG. 229. Papillary carcinoma of the bladder Grade I The villi are delicate and most of the cells are regular, but less than 25 per cent of the nuclei are enlarged and hyperchromatic. $\times 75$.

carcinoma of the prostate gland. It arises chiefly from paraprostatic glands that are sometimes present in the wall of the male trigone, and in

remnants of urachus in the apex of the bladder (Ash). It is composed of large alveoli lined by multiple layers of cells, some of which are usually



FIG. 230. Papillary carcinoma of the bladder. Grade II. The villi are somewhat thicker and atypical nuclei are more numerous. $\times 75$.

columnar. Adenocarcinoma may occur as a flat growth, showing extensive infiltration of the bladder wall, or it may have a thick pedicle and

project into the bladder as a pedunculated tumor, with marked induration of the tissues about its attachment. It always remains relatively flat, however, and its rolled-over edge gives it a characteristic mushroom-like

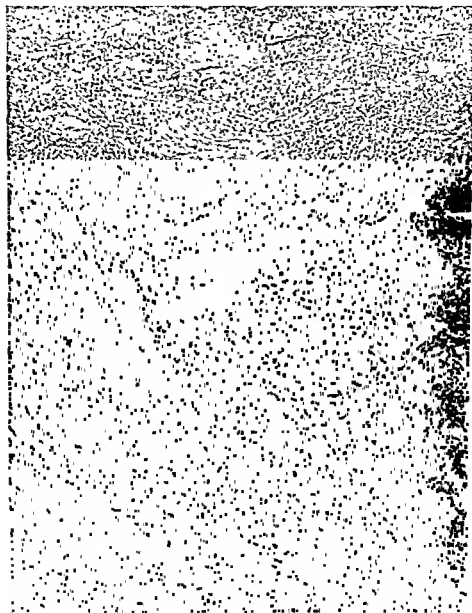


FIG. 231. Infiltrating papillary carcinoma of the bladder, with squamous metaplasia.

appearance. Ulceration occurs early. When found in the vicinity of the trigone or urethral orifice, it is likely to cause obstruction fairly early.



FIG. 232. Infiltrating carcinoma of the bladder. Grade IV. No papillary structure is in evidence. The cells are small, oval, or rounded, with hyperchromatic nuclei, and are scattered in the stroma or concentrated in small, irregular masses. $\times 75$.

Adenomas of the bladder are very rare (24 cases to 1936, Chauvin). They are usually located in the vicinity of the vesical neck or at the apex

of the bladder. The glandular structure of such tumors varies greatly. Some are simple evaginations of the mucosa; some resemble adenoma of the prostate, and may arise from aberrant prostatic glands; some are composed of true mucous glands and are of tubular structure; others are cystic adenomas. They are usually small in size and sessile, though they may be pedunculated. Adenomas are benign.

Sarcoma. Sarcoma of the bladder is rare. Albarran (1892), who had exceptional clinical facilities, observed 2 cases himself and collected reports of 51 others from the literature. McCarthy and Stepita (1929) collected 129 cases, and a number have since been reported. Sarcoma occurs most frequently in the very young or in the aged. Of 75 cases of bladder neoplasms in children, collected by Rathbun (1937), 42, or 56 per cent, were sarcomas.

The vesical sarcoma is a fast-growing tumor, arising, as a rule, on the lateral or posterior wall or on the base, including the vesical neck. It may diffusely invade the wall, or appear as a large polypoid or globular intravesical growth, and cannot be differentiated grossly from carcinoma. Like all sarcomas, those found in the bladder are highly malignant and may quickly progress by direct extension to the neighboring viscera or even to the pelvic bones. All organs, with the exception of the brain, have been recorded as being the site of metastatic growth. Sarcoma is regularly fatal, death being due, as a rule, to the toxic effects of the tumor or to urinary obstruction resulting from pressure of the enlarging growth upon the ureters or, less frequently, by closure of the urethral or ureteral orifices by the tumor's exuberance.

Microscopically, the structure varies, showing spindle-cell, round-cell, or mixed-cell masses through which course thin-walled blood vessels. Numerous cases of myxosarcoma and a few of osteochondrosarcoma rhabdomyosarcoma, and leiomyosarcoma have been reported.

Benign Mesoblastic Tumors. Benign mesoblastic tumors of the bladder are rare. Histologically, they may be classified as follows:

1. Fibroma
2. Myoma
 - a. Fibromyoma
 - b. Leiomyoma
 - c. Rhabdomyoma
3. Myxoma
4. Angioma; hemangioma
5. Neurofibromatosis

Fibromas are most commonly located on the trigone or posterior wall, are slow-growing, and seldom produce symptoms unless they reach unusual size, when they may cause obstruction of the vesical orifice or pressure symptoms. Of the few authentic cases reported, the majority were discovered at operation for other causes or at autopsy. Like fibromas elsewhere, the vesical type is clinically benign, although malignant degeneration is possible. As they occur singly and are usually pedicled, the chance of successful removal is greater than with most vesical neoplasms.

Myomas, fibromyomas, leiomyomas, and rhabdomyomas of the bladder have been reported. *Myoma* of the bladder is histologically identical with uterine myoma. These tumors usually vary from the size of a pea to a weight of several grams, but tumors of extreme size have been reported (a myoma weighing 9,200 Gm., Kresnetki; one weighing 3,200 Gm., Polaillon). Riegel's patient's bladder was filled with a huge myoma. *Leiomyoma* is a rare benign growth of the smooth muscle. It appears as a polypoid tumor, and may reach considerable size. Histologically, it consists of interlacing bundles of smooth muscle fibers with a stroma of connective tissue carrying the blood vessels. Its etiology and pathogenesis have been indefinitely explained on the basis of embryonic rests. The more complex *rhabdomyoma* presents striated muscle, with a cell structure mostly of spindle-shaped cells of small size, varied by larger cells showing striated protoplasm, and many nuclei contained in a central space. It regularly appears early in life and may be regarded as a tumor peculiar to childhood. Only 3 or 4 cases of vesical rhabdomyoma have been reported.

Myxomas may form in the mucous membrane of the bladder at any period of life. In Rathbun's series of 75 primary bladder tumors in infants and young children, 16 were myxomas. Ewing is authority for the statement that polypoid growths in the mucous membrane in any body cavity will usually be found to present many of the characteristics of myxomatous tumors. According to this author, they are chiefly edematous fibroadenomas, or inflammatory hyperplasias, containing little or no mucin. Earlier French writers, notably Albarran and Malherbe, claimed that true myxomas are very rarely found in the bladder, and that, even when found, pathologists would fail to agree as to their histological characteristics. Albarran noted that most of those reported in children were in female infants, and concluded that it was because they protruded through the relatively short urethra that they were more

often located in girls. These soft, smooth, and lobulated tumors seldom ulcerate. They are usually equipped with a pedicle and are regularly solitary. When exposed to the outside air, they shrink rapidly because of their gelatinous and crystalline structure. *In situ*, it is difficult to differentiate tumor tissue from the normal mucous membrane of the bladder wall. Under the microscope, the surface will appear covered with squamous epithelium, beneath which is a loose cellular structure carrying an abundance of good-sized vessels.

Approximately 25 cases of *hemangioma* of the bladder have been reported. Macalpine (1930) reported 2 and reviewed 20 others, some of which lacked histological confirmation. Rathbun (1937) reported a case in a male infant and cited a personal communication from Judd, of the Mayo Clinic, relating to a girl 7 years old upon whom autopsy was performed, revealing a large hemangioma involving the rectum, sigmoid, and bladder.

Neurofibromatosis (von Recklinghausen's disease) occasionally occurs in the bladder. Cases have been reported by Gerhard (1875), Krylieslies (1885), Steden (1923), Heusch (1926), Heidler (1928), and Kass (1932). The disease is characterized by multiple connective-tissue tumors upon the nerve trunks, particularly of the cutaneous nerves. Its occurrence in cavities such as the bladder is unusual. The tumors are multiple, bean-sized, and usually located on the mucosa in the vicinity of the trigone and bladder neck.

The etiology of neurofibromatosis is obscure. Many believe the disease to be congenital, even though it often does not manifest itself until adult life.

Pathologically, these growths differ from ordinary fibromas only in that they always contain nerve fibrils. Symptoms are commonly absent, but obstruction of the bladder neck or ureteral orifices by the tumors may result in urinary difficulties or symptoms of hydronephrosis. *Neurofibromatosis of the skin or other structures may be present.* Cystoscopic inspection should give a good view of the shape, size, and number of the tumors, and should suggest the nature of the lesion even before biopsy is done.

The treatment, in general, is that of other bladder growths, but depends on the number, size, and location of the tumors.

Location of Bladder Tumors. Unfortunately, vesical tumors show a marked tendency to be situated on the bladder base. More than 75 per cent (Report of Registry for Carcinoma of the Bladder, 1934) have

their origin on the trigone, lower portion of the lateral walls, or about the vesical neck, in which situations they are likely to involve the ureteral orifices or, less often, the urethral orifice. Even a small growth, if located near a ureteral orifice, may early cause disturbance of the upper urinary tract. Obstruction at the orifice may result in hydro-ureter or hydronephrosis. This emphasizes the importance of a complete urological examination as soon as a tumor of the bladder is discovered. In many of these cases only a bilateral retrograde pyelogram will reveal the damage wrought by a comparatively innocent-looking nodule in the bladder.

Hidden Tumors. A diverticulum may harbor a vesical tumor, and, when so placed, discovery may be difficult. A tumor thus hidden away may be the cause of obscure hemorrhage. Heslin and Milner (1938), reporting a case of primary carcinoma in a bladder diverticulum, found reports of 29 other authentic cases. Although not a common finding, the possibility of tumor should be considered and growths searched for in all cases of diverticulum.

In greatly trabeculated bladders it is possible for small tumors to be hidden away in the mucosal folds and thus escape detection.

Tumors situated close to the urethral sphincter are often out of range of the ordinary cystoscope; and growths arising in the prostatic urethra, just outside the bladder, are certain to be overlooked unless a urethroscope equipped with a foroblique lens is utilized, so that this portion of the lower tract can be thoroughly scrutinized.

Metastasis and Extension: Recurrence. *Metastasis* to the retroperitoneal lymph nodes or to distant organs occurs late, and is more common in the flat, infiltrating squamous-cell carcinomas than in papillary growths. Various statistics place the incidence of metastases at from 10 to 40 per cent of cases of vesical cancer. Metastases occur either by the lymphatic or hematogenous route, and have been observed in the bones, liver, lungs, regional nodes, and retroperitoneal nodes, but very rarely in the brain.

Direct extension may occur to the prostate, pelvic tissues, or up the ureter toward the kidney. Extension to the rectum or vagina is uncommon. Extension occurs late, and true cancerous cachexia from generalized spread of the disease is rare.

Recurrences are very frequent in all types of bladder tumor, and this tendency to recurrence offsets the advantages of late metastasis and the tendency of the tumors to remain confined within the bladder for con-

siderable periods. Following removal of a papilloma or papillary carcinoma, there may be recurrence at the same site or elsewhere in the bladder. The removal of a benign papilloma may be followed by the development of a papillary carcinoma at the same site, or by a diffuse involvement of the entire mucosal surface. Secondary deposits are likely to occur where the mucosa comes in contact with malignant areas when the bladder is relaxed and more or less folded upon itself.

Complications. The complications of tumors of the bladder are hemorrhage with anemia, cystitis and pericystitis, hydronephrosis and pyonephrosis from ureteral obstruction and infection, and septicemia. Frequently death occurs not from the bladder tumor itself but from urosepsis following obstruction of the ureter and pyonephrosis.

Sex and Age Incidence. In all tumors of the bladder, whether benign or malignant, there appears to be a marked preponderance of occurrence in the male sex (4 to 1, Lazarus and Rosenthal, and Beer; 2 to 1 in infants, 5 to 1 in adults, Deming; 3 to 1 carcinoma, Rauenbusch; 3 to 1, sarcoma, Rabson).

Epithelial growths may arise at any period of life, but are very rare in children and most common after middle life, especially in the sixth decade. While all types of tumors have been recorded as occurring in children, over one-half have been sarcomas.

Etiology of Bladder Tumors. Little is known regarding the origin of bladder tumors. The most commonly held theory is that continued irritation is an important causal factor in their production. There is a well-founded suspicion in the minds of many observers that chronic cystitis, especially the encrusted variety, disposes to the growth of vesical tumors; and the same is true of vesical calculus. The likelihood of carcinoma forming in an exstrophied bladder, where the mucous membrane is subjected to extraordinary exposure, is well recognized. Stoerk, Cahen, and others have traced a definite relation between cystitis cystica and multiple papilloma; and Ewing is of the opinion that the tendency to multiplicity of villous carcinoma and the heterotopic recurrences indicate the existence of widespread lesions in the mucosa, from which tumors may develop. Bilharzial infestation has been shown by numerous observers to favor the development of vesical tumors—both carcinoma and sarcoma—the tumor apparently being superimposed upon the bilharzial lesion.

The frequency of cystitis, papilloma, carcinoma, and even sarcoma among workers exposed to aniline and certain other chemicals has been

pointed out and investigated by a large number of workers. Interesting observations, made during routine cystoscopic examination of men exposed to the fumes of aniline dyes, have been published by those in charge of the medical supervision of employees of the Dupont interests at Wilmington, Delaware. From other plants where dyes are handled have come reports that measures to prevent workers from being exposed to the irritating fumes have markedly reduced the incidence of bladder tumors. Vesical papilloma and papillary carcinoma have been produced experimentally in animals exposed for long periods to irritating fumes, such as those of naphthylamine. Gehrman, Wolfe, Evans, and others found tumors of the bladder as an occupational disease in workers exposed to benzidine, alphanaphthylamine, betanaphthylamine, and other nitro and amino compounds, but not in those exposed to aniline. Constant exposure to the carcinogenic agent appears to be the important factor in the development of bladder tumor and of multiple papillomatosis; but thus far, neither the carcinogenic agent nor the mechanism of action in the production of the tumors has been shown. Evans, in an analysis of 85 cases, found that the majority of the tumors appear after from 6 to 20 years of exposure, the average time being 12 years; and that while the incidence is higher in persons from 40 to 60 years of age, an appreciable number occur in those from 30 to 40 years. No particular portion of the bladder appears to be especially susceptible, but, as with vesical tumors in general, a large proportion are found in the vicinity of the ureteral orifices. In other cases, a diffuse papillomatosis is present. The majority of so-called "aniline tumors" are malignant. The histology, symptoms, and treatment of these tumors do not differ from those of other vesical neoplasms.

Kirwin has recently advanced the interesting theory that papillomatosis of the bladder is due to a filterable virus—a concept that he bases on the work of Wile and Kingery (1919) on the etiology of common warts, and on the later investigations of Beard and his coworkers on the etiology of the so-called "Shope rabbit papilloma," a growth known to be caused by a virus.

Wile and Kingery obtained typical lesions of verucca at the point where they injected a filtrate made from curetted wart material, and concluded that these results definitely showed that such changes can be caused by a filterable virus, and that "when trauma and foreign bodies apparently are present as exciting factors, they may merely represent the point of entrance of an infectious agent." Vesical papillomas have much in com-

mon with warts upon the cutaneous surface; and the empty bladder lies in folds everywhere apposed, so that it presents ideal conditions for contact infection could it be established that these neoplasms have an infectious origin.

In 1934, Rous and Beard, studying the etiology of the virus-induced rabbit papilloma at the Rockefeller Institute, observed: "Implantation growths of the papilloma in favorable hosts have the morphology of epidermoid tumors of greater or less malignancy. They behave as these do and elicit similar changes in the surrounding tissue." Two years later, Rous, Beard, and Kidd, after further investigations, stated positively that "the virus-induced papilloma is not only a neoplasm in its immediate aspect and habit, but sometimes one that verges on malignancy." Recently, Beard and his coworkers at Duke University have succeeded in demonstrating that a "specific material" exhibiting the biological characteristics of the virus responsible for rabbit papilloma could be obtained from extracts made from the growths themselves.

Kirwin feels that the findings of these two groups of investigators on the etiology of common warts and the so-called "rabbit papilloma" lend strong support to his belief that bladder papillomatosis may be due to a filterable virus.

Symptoms. The symptoms of bladder tumor are in no way pathognomonic. Hematuria, which is usually painless, is the initial symptom in over 80 per cent of cases, and may long remain the only symptom. As this is common to many urological conditions, it emphasizes the great importance of making an early and thorough cystoscopic examination of every patient with blood in the urine. Kretschmer, analyzing the cause of hematuria in 933 cases, found the bleeding to be due to bladder lesions in 307 patients, more than 75 per cent of whom had tumor. Bleeding is usually intermittent, but in a small number of cases is constant. The hematuria may be very slight, or the urine may be grossly bloody.

In papillary tumors the bleeding is more likely to occur early in the disease than in the solid infiltrating carcinomas. The rare benign non-papillary tumors do not, as a rule, produce hematuria until late. Even when such a tumor is attacked by erosion and ulceration, the bleeding is usually negligible until the lesion is far advanced. By their size and location, however, these tumors may cause symptoms of urinary obstruction.

Urinary difficulties, such as frequency, urgency, tenesmus, and drib-

bling, due to an associated cystitis or encroachment of the urethral orifice by the tumor, are not uncommon complaints; these, however, usually occur later than hematuria. Growths located near the internal sphincter or upon the trigone cause urinary disturbances much sooner than tumors upon the posterior or anterior wall.

Occasionally the earliest symptoms are referable to the kidneys, due to the common involvement of one or both ureteral orifices in the pathological process. Impairment of renal function is present in about a third of the cases.

Diagnosis. The chief steps in the making of a diagnosis of bladder tumor are: (1) the history, (2) physical examination, (3) cystoscopy, (4) cystography, (5) biopsy, (6) study of the pathologist's report and determination of the type of tumor.

The history should be carefully elicited. Age and sex have a certain bearing, for bladder tumors are seen most often between the ages of 45 and 60 years, and are 4 times as frequent in men as in women. Previous residence in a tropical country where bilharziasis is prevalent, or prolonged contact with synthetic dyes or certain chemicals may be significant.

The physical examination is important, for the existence of complications elsewhere in the body will influence the choice of treatment should vesical tumor be found. Bimanual palpation should never be neglected. Rectal or vaginal examination may reveal infiltration of the bladder wall which the cystoscope fails to show.

Cystoscopic examination is the most important procedure in the diagnosis of bladder tumor. The ordinary cystoscopic examination, however, is often misleading. Though the foroblique lens system helps to show the tumor in its actual proportions and in proper relation to surrounding structures, no urologist should consider himself properly equipped unless he can also command a retrograde and a right-angle lens system, enabling him to view the tumor in all its aspects.

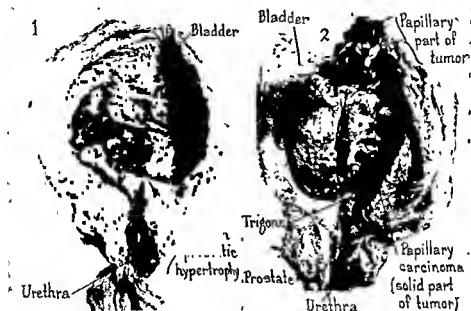
The bladder will not infrequently be so contracted or irritable, or the field so obscured by bleeding, that a good cystoscopic view is impossible.

Cystoscopy enables one to establish (1) the source of the hematuria, (2) the presence or absence of tumors of the bladder, (3) the number, location, and character of the tumors. It also enables one to secure a specimen from the tumor for microscopic study.

In most cases the cystoscopic picture of vesical neoplasm is unmistakable (Plate IV). The cystoscopist should familiarize himself with

the appearance and pathological characteristics of the various types of bladder neoplasms. This can be attained only by constant practice and wide experience, but from the outset it should be the aim of all who attempt the treatment of bladder tumors.

Papillomas are more often multiple than single, but there is no fixed rule. The typical papilloma appears as a fine, branching tendril attached by a delicate pedicle to the bladder wall—usually the lower lateral or posterior wall. The delicate grayish-pink branches float about in the irrigating fluid, giving an appearance of seaweed or a branching plant.



The resemblance to seaweed is further enhanced by the fine capillaries which can be seen coursing through the fronds. The papillary fronds are usually pointed, unless there is associated cystitis, when they may be edematous and rounded or even necrotic. Other types of papilloma are the firmer, less branching "raspberry" growth, which is attached to the wall by a broader pedicle, and the distinctly sessile tumor with a broad base but without infiltration of the base or adjacent vesical mucosa.

The pedicle of a carcinoma and the adjacent bladder wall are regularly infiltrated—an important diagnostic point when differentiating between

benign and malignant growths. It is not always possible to view the base of the papilla, however, nor to determine the presence or absence of infiltration.

Flat, infiltrating tumors are also seen. The surrounding mucosa will be thickened and trabeculated, and the whole aspect of the neoplasm nodular, presenting a solid, fleshy appearance quite different from the delicate branching fronds of the typical papilloma.

Adenocarcinomatous tumors, which are more solid, may yet be partly papillary, and under such circumstances the basal infiltration will be more plainly evident. Again, the picture may be one of encrusted ulceration, with extensive granulation or a film of mucus. There may be several such areas, interspersed over a red and angry-looking mucosa.

One cannot interpret the cystoscopic picture correctly between a benign papilloma and one of low-grade malignancy. Between the characteristic benign papillary growths and the frankly malignant tumors is a host of borderline cases, showing various gradations and mergings of the papillary and solid forms. Even the most expert may find it hard to estimate the relative malignancy of some of these, and recourse should be had to all the diagnostic aids at the urologist's command.

The cystoscopic appearance of the rarer non-epithelial tumors represents an almost infinite variety. The benign non-papillary tumors may reach considerable size before producing symptoms, and rarely show necrosis and hemorrhage until late. The rare sarcomas developing in older people may seldom be differentiated cystoscopically from carcinomatous tumors. If a glistening, shiny, and smooth neoplasm is seen, a mesothelial tumor should be suspected.

A few well-recognized vesical lesions may closely simulate the cystoscopic appearance of neoplasm: bullous edema, tuberculosis, tertiary syphilis, and ulcerative and granulomatous lesions associated with chronic infections. Encrusted phosphatic cystitis may simulate infiltrating carcinoma.

Cystography, by revealing any filling defects or irregularities in the outline of the bladder, gives valuable information regarding the location and extent of the tumor in cases where cystoscopy is impossible; or it may confirm the cystoscopic findings. At the Brady Foundation, in the New York Hospital, both *umbrathor* and *diodrast* are used as contrast media. *Umbrathor* (p. 173), which is flocculated as a surface coating upon the mucosal lining, gives an especially good relief picture of any

irregularities in the outline of the bladder shadow. Cystography is also useful in showing the degree of infiltration of the wall. The normal portion of the wall distends smoothly and evenly; but the infiltrated portion does not distend, an indentation appears, or this portion will be seen closer to the median line. On the other hand, a papillary growth which has not infiltrated the wall permits distention of the underlying wall and, at the same time, projects into the vesical cavity. In such cases the bladder outline may be spherical.

Vesical neoplasms can also be differentiated by the roentgen rays after filling the bladder with air. Cystography, or pneumocystography, is particularly valuable when the urethra is obstructed, or when hemorrhage is so severe that cystoscopy is impossible. It also serves to amplify and confirm the cystoscopic findings.

A *biopsy specimen* is secured with a cystoscopic rongeur, such as the Lowsley or Kirwin rongeur, and subjected to histological study, to determine the structure of the tumor and its *grade of malignancy*. The specimen should preferably be taken from near the base of the tumor. One part of a growth is not always typical of the entire growth. A specimen taken from a tendril of a papillary tumor, with no portion of the tumor base included, may show only benign changes; whereas examination of a specimen from the base or pedicle, or from another tendril of the same growth, may show definite cell atypism and malignant infiltration. Where doubt as to the extent and degree of malignancy exists, therefore, several sections should be taken from as widely separated areas as possible.

In the presence of excessive hemorrhage, preliminary cauterization will help to clear the field, without complicating any later procedure, since treatment, in any event, must be applied to the base of the tumor.

The pathologist's findings should be carefully correlated with those of the physical examination, cystoscopy, and cystography, in order to select the *method of treatment best suited to the particular case under consideration*—whether by surgery, diathermy, irradiation, or a combination of these methods.

Prognosis. The prognosis of any form of bladder tumor cannot be regarded as cheerful, though many instances of apparent cure are on record. The early benign growths are easily removed as a rule, but they recur with discouraging frequency, either at the site of the original tumor or at another site, and these recurrences are more than likely to prove malignant. The unfavorable results in cases of vesical tumor are due

largely to late diagnosis and this tendency to recurrence following removal.

The prognosis of malignant tumors depends upon the size and location of the growth and the extent of infiltration. A small tumor of low-grade malignancy involving a ureteral orifice may already have caused destruction of a kidney when the patient is first seen; whereas a larger tumor of a higher grade of malignancy, located higher up on the lateral wall, where it does not involve the ureter, may be radically excised with a good chance of cure. Deeply infiltrating solid growths are rarely cured except by wide excision or total cystectomy. Malignant papillary tumors may recur in the form of flat carcinomas. With sarcoma, the prognosis is always extremely grave, very few of these patients surviving for any length of time, no matter what the treatment administered.

Treatment. The treatment of vesical tumors, either by surgery or radiotherapy, is admittedly unsatisfactory. The various methods in present use are based on three distinct types of treatment: surgery, fulguration or removal with the resectoscope, and radium or x-ray irradiation.

Because of the great variety and disposition of bladder tumors, it is impossible for the therapist to limit himself to one method of treatment in all bladder growths. No one agent or method is applicable to all cases. The number, location, histological structure, and stage of advancement of the tumor all influence the choice of treatment; and only careful study of all the findings of examination in a given case, and familiarity with the various methods of approach, will enable one to choose wisely the method best suited to the particular case under consideration.

For benign papilloma, fulguration through the cystoscope or through a cystotomy wound has been the standard method of treatment, but recurrences have been discouragingly frequent.

In accordance with his theory that vesical papillomatosis is an infectious condition, Kirwin has of late treated a number of these cases by excision of the growths with the wire-loop electrode, cauterization of the bases with the ball electrode, and sterilization of the bladder mucosa by the application of a 50 per cent solution of phenol in glycerine, followed by alcohol 95 per cent, when the phenol solution has been in contact with the mucosa for about 3 minutes (see p. 1146). In the few cases in which this method has been employed to date, the results have been definitely superior to those achieved by the older methods.

The majority of malignant tumors and the so-called "borderline cases" are probably best treated by one of the following methods:

- (1) Suprapubic radical resection of the tumor (sometimes with implantation of a ureter higher up on the bladder wall or into the skin):
 - (a) by scalpel (using clamps), followed by deep x-ray therapy
 - (b) by cautery knife, with radon implantation before the wound is closed
- (2) Fulguration by loop, ball, and disc electrodes through a suprapubic incision, followed by implantation of radon seeds
- (3) Closed method: removal of the exuberant portion of the growth by the resectoscope, followed by transurethral implantation of radon seeds and, in some cases, external x-ray therapy
- (4) Total cystectomy, with transplantation of the ureters
 - (a) into the skin of the loin or groin
 - (b) into the bowel

Small, superficial papillary carcinomas with little or no infiltration often can be treated by transurethral electrocoagulation of the exuberant portion of the growth, followed by transurethral implantation of radon seeds. The Kirwin or other resectoscope may be used for the removal of the body of the tumor, or simple fulguration may be employed. The important feature is the removal of the projecting mass, so that the base may be fully exposed for radon implantation. Kirwin has designed a measuring instrument, to determine the dimensions of the tumor to be treated, and also an implanter, by means of which radon seeds may readily be introduced into bladder tumors by either open or endoscopic routes (Radium and Roentgen-Ray Therapy of the Genito-Urinary Tract, p. 1751).

For papillary carcinoma with definite infiltration, and for solid, deeply infiltrating carcinoma, complete surgical excision of the tumor, when possible, is the treatment of choice. Because an electric wound in the bladder wall does not heal well, we think it wiser to excise a bladder tumor with a scalpel, cauterizing the surface with carbolic acid followed by alcohol, rather than to use the electrocautery for excision. There are others, however, who prefer the electric knife. Involvement of a ureteral orifice may necessitate implantation of the ureter to a place higher up on the bladder wall or into the skin of the loin or groin.

If an infiltrating tumor is not surgically removable, it should be treated by removal of the exuberant portion of the tumor by the loop electrode,

through a suprapubic incision, followed by the implantation of radon seeds. After the tumor mass has been scraped away by means of the loop electrode, the disc electrode is applied to the exposed base, thus leaving a smooth surface into which radon seeds can be introduced with a minimum of effort.

Total cystectomy and bilateral ureteral transplantation is sometimes advisable in papillomatosis that cannot be controlled by fulguration, and in extensive tumors in the lower bladder segment involving the ureteral orifice or the urethra, providing the patient has satisfactory kidney function and a normal ureter and pelvis on one side at least, and is proved free of metastasis. The ureters are transplanted to the bowel or to the skin of the loin or groin.

Tumors of a diverticulum are best handled by surgery (Figs. 246 to 248).

While the use of radium and roentgen-ray therapy has proved a valuable adjunct to other methods employed in combating bladder tumors, irradiation therapy alone has not been satisfactory. This is admitted by practically all therapists. External roentgen-ray therapy has a certain usefulness (1) in the control of symptoms after operation, (2) in inhibiting the growth of new tumors of low grading after operation, (3) in controlling persistent and annoying hemorrhage. Used preoperatively, it may be that x-ray therapy shuts off the lymphatic and vascular supply, so that, at operation, there is a better chance of extirpation of the malignancy.

These various procedures are discussed under Resection of the Bladder Wall for Malignant Tumor (p. 1106); Fulguration of Bladder Tumors (p. 1146); Radium and Roentgen-Ray Therapy of the Genito-Urinary Tract (p. 1750).

Bladder Tumors Originating in the Urachus

A distinction should be made between the more commonly seen papillary and solid tumors of the bladder and the rare colloid adenocarcinoma, found in the vault of the bladder, which arises from the epithelium of the urachal canal. As pointed out by Begg, of New Zealand (1930), the importance of making this differentiation "lies in the consideration that what presents itself under the guise of bladder tumor is in reality not a bladder tumor at all, and any attempt to treat it as such by the usual methods—fulguration, radium, etc.—is predestined to failure; whereas

early recognition of the true condition offers the patient at least a hope of effective cure by surgical means."

Pathology. Most of the tumors seen at the apex of the bladder are adenomatous or adenocarcinomatous in type. When viewed through the cystoscope, they are taken for the more commonly occurring papillomas; but the pathologist, on examining the excised specimen, will find it to have undergone colloid or mucoid degeneration, yet still to retain ducts, lined by columnar epithelium with scattering goblet cells, which are filled with mucin, in close resemblance to the typical adenocarcinoma of the rectum.

Papillomas of the ordinary type may appear at the apex, though this is rare; and adenomas or adenocarcinomas, with or without mucin-formation or degeneration, may occur in any part of the bladder, without relation to the urachus. Although a true tumor of the urachus does not necessarily appear at the site of this structure's insertion into the bladder, the characteristics of apical vesical tumors of urachal origin are so definite that there is no difficulty in differentiating them from the colloid cancers of the bladder wall itself. The urachal tumor regularly arises in the outer muscular layer of the bladder wall and only secondarily makes its entrance into the vesical cavity.

Differential Diagnosis. Differential diagnosis will not be difficult if the examiner keeps in mind the fact that urachal tumors always appear at the apex, either completely outside the muscular wall or no further in than the muscular layer, only secondarily penetrating to the bladder cavity, or, perhaps, merely producing a hudge of the mucosal surface. Genuine bladder neoplasms ordinarily take their origin in the mucous membrane, advancing to the muscular tissue only when the disease has progressed extensively. Such tumors are generally furnished with pedicles, while urachal tumors are never pedunculated.

Symptoms: Prognosis: Treatment. The symptoms of urachal tumors, as well as their clinical course and amenability to treatment, are similar to those of any solid vesical tumor. Granted that they are usually malignant, the prognosis is as good, and possibly a trifle better, than that we have been led to expect in neoplastic disease of the bladder. A review of the published cases and statistics gives the impression that surgery has been, on the whole, the most satisfactory method of treatment.

Herniation of the Bladder

True herniation of the bladder through the inguinal or femoral rings is of infrequent occurrence. (In comparison with intestinal hernia, it is very rare). Inguinal hernia is by far the more frequent, and is seen much oftener in men than in women. Femoral hernia is usually seen in women. Very rarely there may be protrusion through the obturator foramen, or a ventral hernia.

Incidence and Etiology. Bladder hernia may occur at any period of life, but is more prevalent in later adult life. Factors that may cause herniation of the bladder in susceptible persons are: weakness of the abdominal wall, either congenital or acquired; trauma from any cause, inducing increased intra-abdominal pressure; superabundant prevesical fat, exerting traction on the bladder and causing it to protrude downward through one of the hernial openings; urinary obstruction overdistending the bladder; old age or debilitating disease, resulting in flaccidity and atony of the abdominal wall. The most common predisposing factor in women is pressure of the gravid uterus during the final months of gestation. In males, the bladder normally approaches the inguinal fossa more closely, and vesical hernia will be more often associated with the direct type of prolapse.

Several years ago, through the courtesy of Doctors Burdick and Coley, of the Hospital for the Ruptured and Crippled, in New York, we were able to study 15 cases in which the bladder was found occupying a hernial sac. Of these 15 cases, 7 occurred on the left side, 6 on the right, 1 was bilateral, and in 1 the side was not mentioned. There were 3 femoral hernial sacs presenting a portion of the bladder. Eight of the patients were males, 7 females (2 of these had femoral hernias). Seven patients were under 10 years of age, and only 2 were over 40 years. The fact that the herniation in this rather large number of cases was accidentally discovered at operation emphasizes the importance of bearing in mind the possibility of vesical herniation and making diligent search for the condition.

Types of Vesical Hernia. A vesical hernia may be extraperitoneal, intraperitoneal, or paraperitoneal.

In the *extraperitoneal* type of vesical hernia there is protrusion of the anterior or lateral extraperitoneal wall of the bladder (usually with the superabundant prevesical fat) into the inguinal or femoral canal. This type of hernia is ordinarily small. It often produces no symptoms, and

may be discovered only at operation or autopsy. In form, it is always a direct inguinal hernia.

The *intrapertitoneal* hernia is usually secondary in type, and is regularly inguinal. The hernial sac may consist of the entire bladder with the exception of the trigone, or of part of the bladder, a diverticulum, or prevesical fat alone, but it is covered with peritoneum. When a smaller part of the bladder is involved, the sac may contain loops of the small intestine with a portion of the omental covering, or, in women, the uterus, ovaries, fallopian tubes, and ureters. In men the prostate is sometimes involved.

Parapertitoneal hernia may take the form of either a direct or an indirect hernia. In either case, the bladder will be found on the inner side of the hernial sac, the serous covering of its superior surface forming the inner wall of the peritoneal sac. This is the easiest type of vesical hernia to handle successfully. It is also, fortunately, the most common. With the bladder in the inner posterior part of the hernial sac, it is a comparatively easy matter to free the sac from the spermatic cord elements by gauze dissection, and thus discover the bladder before there is a chance of injuring it because one is unaware of its participation in the hernia. Except in very old or infant patients, the bladder in this type of vesical prolapse will be found enveloped in a thick layer of fat. This superabundant fat is believed by some observers to play an important role in the production of the hernia.

Symptoms and Diagnosis. The most common complaint is of a "rupture" or "tumor" in the inguinal or femoral region. The patient may give a history of "two-stage urination"—that is, of first evacuating the urine in the non-prolapsed portion of the bladder and, later, that in the herniated portion; or he may have noted that pressure on the "tumor" is necessary to effect complete evacuation of the urine, and that such pressure is followed by reduction in the size of the tumor. As a rule, an unstrangulated vesical hernia causes little discomfort unless secondary infection takes place, and the condition is frequently not recognized except at operation or autopsy. Strangulation of an inguinal hernia is a fairly common occurrence, but a strangulated femoral hernia is rare. The clinical picture varies according to what structures are strangulated with the bladder. Should a ureter be thus involved, symptoms of urinary obstruction will be in evidence, and to these may be added gastrointestinal manifestations such as sometimes complicate renal obstruction from other causes.

Physical examination may give no intimation of anything save a typical inguinal or femoral hernia. "Two-stage urination" is suggestive of vesical involvement. The possibility of a diverticulum of the bladder must still be considered; and in men of middle age, a rectal examination should always be made to distinguish the symptoms from those produced by an hypertrophied prostate. Heineck (1921) noted that if a hernia still feels doughy, after reduction of the palpable mass following evacuation of the bladder, one is probably palpating prevesical fat. Any irreducible hernia should be suspected of containing a portion of the bladder until its presence can be positively ruled out. Transillumination will differentiate the condition from hydrocele, for a herniated bladder is not translucent; but this does not rule out varicocele, inflammatory glands, or neoplastic growth, none of which is translucent. By passing a sound through the urethra and determining whether its tip is within the hernia, the presence of a portion of the bladder therein can immediately be demonstrated. Passage of a catheter will quickly show whether the size of the swelling decreases as the bladder is evacuated; and the reverse can be shown by injecting air or fluid through the catheter and noting whether the tumefaction increases in size. If this is followed by cystoscopic inspection, the presence of vesical hernia will, in most cases, be adequately demonstrated.

A positive diagnosis of vesical hernia, in suspected cases, can be made by cystography.

Prognosis. The prognosis is favorable if the bladder can be returned to its normal position without being injured, and before serious complications have set in.

Treatment. Treatment is surgical—reduction of the hernial sac and repair of the defect in the bladder wall. The location of the hernia will, of course, influence the choice of operation. If strangulation has occurred, the treatment must include measures for combating shock, and the operation performed only when the patient's condition is such as to permit it with reasonable safety.

Frequently, participation of the bladder is not suspected in connection with an inguinal hernia until operation for the hernia has been undertaken. If only a small part of the bladder has herniated, this portion can be separated from the peritoneal sac by gauze dissection and invaginated into the abdomen. Recurrence can be prevented by setting a purse-string suture in the floor of the inguinal canal.

For more extensive participation of the bladder in a hernial sac, a

more elaborate procedure is required. The bladder hernia should always be dealt with before the regular procedure for the cure of inguinal hernia is carried out.

Prolapse of the Bladder Through the Urethra

In the female, the bladder may herniate through the urethra. Greatly relaxed sphincters, and relaxation or weakening of the ligaments which support the bladder in position, added to some unusual force, such as straining at stool, are responsible for the prolapse. The condition is rare. Unless reduced promptly, gangrene of the bladder, due to the shutting off of the blood supply, may result.

Treatment. Treatment consists of reduction of the prolapsed bladder and the institution of measures to prevent recurrence of the herniation.

Cystocele

Cystocele is a protrusion of the bladder into the vagina. It is due to a relaxation of the normal pelvic supports, allowing the bladder to present itself in the vagina as a bulging, soft, fluctuant mass. It is frequently associated with rectocele and displacement of the uterus.

Etiology. Cystocele is an aftermath of prolonged, difficult labor. Davies, who exhaustively studied the anatomopathological aspects of cystocele, concluded that an injury to the pubocervical ligament, as well as the anterior wall of the vagina, is essential to its formation. An overstretched vagina, he believes, is capable of normal involution, because of the many involuntary muscle fibers in its wall, *unless* the supports of the bladder have been so distorted that they are constantly pulling the vagina out of position. Such a situation will shortly bring about a weakening of some portion of the vaginal wall, permitting herniation of the bladder through this weak spot.

Symptoms and Diagnosis. The chief complaints are of the mass presenting itself in the vagina, urinary frequency, and, occasionally, obstruction to urination.

The diagnosis is easily made by observing and palpating the mass, and by the cystoscopic appearance. The urethra, being fixed in its normal location, is high above the ureteral orifices, which descend with the bladder. In order to observe them, therefore, the eye-piece of the cystoscope must be considerably elevated.

Prognosis. The condition is not relieved by ordinary palliative means. Operation is not always successful, but should be attempted when the symptoms are distressing.

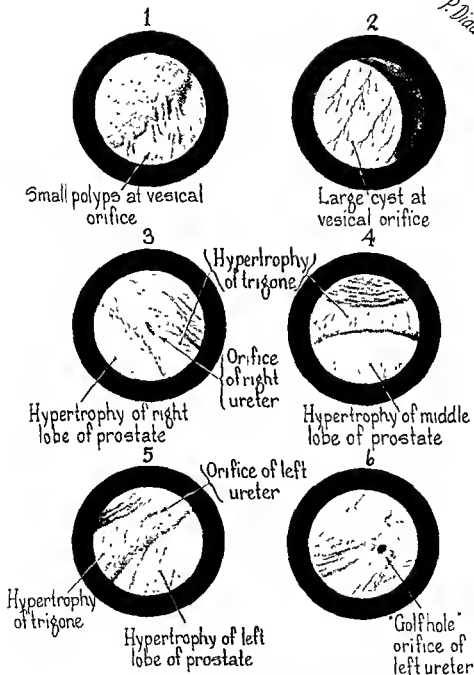


PLATE V. CYSTOSCOPIC APPEARANCES IN CERTAIN PATHOLOGICAL CONDITIONS OF THE VESICAL NECK AND TRIGONE

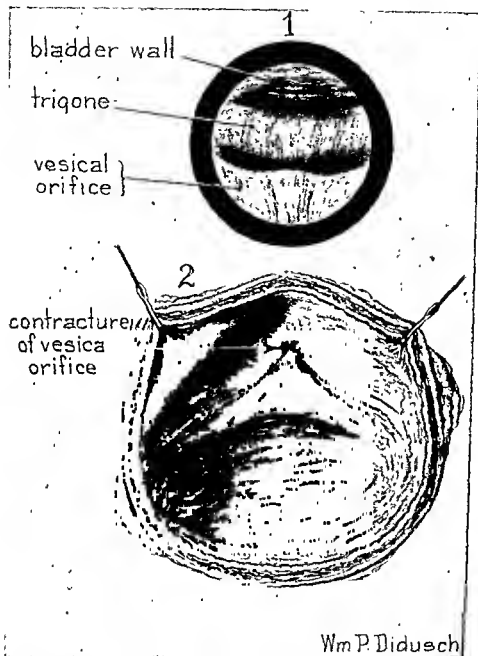


FIG. 234. Contracture of the vesical neck. (1) Cystoscopic view of the contracture. (2) View of the opened bladder from above.

normally. To meet the increased strain upon it, the muscle undergoes compensatory hypertrophy. This results in vesical irritability, frequency, urgency, and even vesical spasm, which is the detrusor's way of resenting the foreign body which the enlarged trigone simulates.

If the trigonal hypertrophy is associated with enlargement of the median lobe of the prostate, these two hypertrophied structures may form a continuous mass raised above the level of the surrounding mucosa, and eventually bring about complete inability to empty the bladder. The outward passage of urine will be blocked by a wide, transverse barrier in the bladder floor behind the urethral orifice. If the condition is allowed to persist long enough, the retained urine may undermine the trigone and form a sort of valve with a deep pouch behind it—the trigone acting as a septum, which shuts off the flow of urine.

In *postmortem* studies it has been observed that the enlargement is always greatest in cases presenting elevation of the dorsal portion of the vesical orifice. In cases where the median lobe was enlarged and somewhat off-center, the trigonal hypertrophy tended to be asymmetrical and most marked on whichever side of the vesical orifice was the lower; but when the lobe was centered, it acted as a ball-valve, and the hypertrophy would be symmetrical.

There are characteristic stages in the development of trigonal hypertrophy. When first in evidence, the trigone is but slightly raised above the surrounding mucosa, though the interureteral ridge shows a definite elevation. A little later, the trigone will have been pushed up to the level of the interureteral ridge and ligament, and there will be a shallow pouch behind them, which gradually grows deeper. After the median bar is definitely formed, the trigone appears as a shelf behind the bar.

Treatment. The hypertrophied trigone may be removed suprapubically or transurethrally (*Operative Treatment of the Bladder*, p. 1145). If observed early, before it has become obstructive, removal of the primary cause of urinary obstruction, such as a median bar, may make treatment of the trigone unnecessary.

Vesical Calculus

Incidence and Etiology. Most vesical calculi probably originate in the kidney. A renal stone, or the nucleus of a potential stone, that has passed through the ureter into the bladder, is usually evacuated, especially by the female. Should the stone or nucleus be retained in the bladder, it is almost invariably because of some associated abnormality causing obstruction to urinary evacuation (prostatism, cord bladder, urethral stricture, vesical diverticulum). These stones are usually found in older men (rarely in women), are generally of small size, and frequently are multiple. The majority of vesical calculi are predominantly uric acid or urates.

Primary bladder stones in the United States are mostly formed about a foreign body retained in the bladder, such as an unabsorbed suture or a fragment of catheter, filiform, sponge, drainage tube, or splintered bone, or a hairpin, bit of glass, needle, or other object introduced or swallowed by the patient. In Europe and the Western Hemisphere the incidence of vesical calculus is low in comparison with that of stone originating in the upper tract. However, in certain other sections of the world, notably



FIG. 235 Photograph of a large calculus removed from the bladder by operation. After removal, the stone was broken. The lower picture shows the nucleus.

South China and India, the incidence is very high. The variations of incidence in different parts of the world are undoubtedly due in large part to differences in diet and mode of living.

Siddall, in his study of the high incidence of bladder calculus in comparison with renal stone in South China, advances this explanation:

"The habits of eating, drinking, and working in South China supply the fertile soil in which primary vesical stones are easily grown. The urine is concentrated, and there are present in relatively large amounts uric acid and oxalates. It is pos-

sible that the factor which actually plants the seed or nucleus of the stone is recurrent albuminuria. It has been shown by Nicols and Hoecker that strenuous exercise can cause at times a severe albuminuria in normal subjects. If this is true, the Chinese farmer who works hard with his hands must have recurrent waves of albuminuria just at the time when factors are operating to increase the excretion of endogenous uric acid. . . . This albuminuria may disturb the protective colloids in the urine, causing the uric acid and oxalate to precipitate out. . . . A certain amount of stagnation of the urine is required (for stone formation) and the most likely place is the bladder instead of the kidneys."

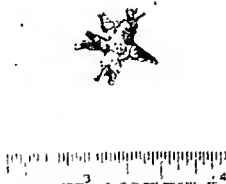


FIG. 236. Photograph of a "jack-stone" removed from the bladder by suprapubic cystotomy.

Etiological factors that have been advanced for the formation of stone include: climate, heredity, racial proclivity, dietary deficiencies or imbalances, endocrine disturbances. These are discussed under Renal Calculus (Etiology, p. 1584).

That vesical calculus is fundamentally a deficiency disease is indicated by its diminishing frequency in childhood in countries where there has been a substantial general improvement in the diet of infants and children. In the United States and England this improvement has been striking. Vesical calculus in childhood, once a common occurrence, is now infrequent in these countries. Twinem, in a study of 306 patients with vesical calculus operated upon in the New York Hospital in the 117 years between 1820 and 1937, found that the percentage of patients under 30 years of age decreased from 83.3 per cent in the first 25 years to 10.9 per cent in the last 25 years. Of the 129 patients operated upon for vesical stone between 1921 and 1927 at the Brady Foundation, only 1 was under 10 years of age and only 2 between 10 and 20 years, while 75

were between 50 and 70 years. This shift in age distribution has also been noted in England and certain other European countries. (There is one type of vesical calculus, however,—the rare xanthine stone—that appears to occur much more frequently in young subjects.) In India, where dietary habits have not changed, vesical calculus in patients under 20 years of age is still very common and shows little decrease in frequency.

Hyperparathyroidism is also believed to play an important role in the production of urinary lithiasis. The stones in these cases are usually multiple. The increase of hormone upsets the metabolism of calcium and phosphorus, resulting in an abnormally increased concentration of these salts in the urine, with subsequent formation of urinary calculi.

Important accessory factors in the formation of vesical calculi are the reaction and concentration of the urine, urinary retention, and infection.

Any condition which causes retention, so that residual urine is constantly present, will strongly influence the precipitation of salts, with the tendency to subsequent calculus-formation. The hypertrophied prostate is, perhaps, the best example of such a retention-producing condition; and the importance of prostatism in the production of vesical stone is indicated by the fact that in the United States and Europe vesical lithiasis is becoming increasingly a disease of the older male, being relatively infrequent in women and in children. If the bladder cannot be completely emptied at each micturition, small potential nuclei, which have descended from the kidney and which would be easily evacuated by a normal bladder, will be retained and may form vesical stones. These nuclei are usually composed of uric acid, oxalate of lime, and sodium and ammonium urates. If retained in the bladder, they may rapidly increase in size—phosphates, urates, and more uric-acid deposits adhering to them. The influence of stasis is also shown by the relatively high incidence of stone in vesical diverticula and the fairly frequent occurrence of urinary calculi in patients immobilized in bed for long periods because of traumatic injuries or bone disease.

The exact relation of infection to the formation of vesical calculus is undetermined. Stones formed in uninfected urine are common. Urinary-tract infections without stone are also common. It is definitely known that certain types of infection, such as that produced by the *Bacillus proteus* or the *Staphylococcus albus*, induce alkaline decomposition, which has long been recognized as favoring the production of stone. When alkaline decomposition occurs, the phosphates of calcium,

ammonium, and magnesium are not held in complete solution, so that the likelihood of their being deposited is great.

Pathology. *Mechanical irritation of the vesical mucosa from contact with the stone during each micturition results in a chronically inflamed bladder.* Depending on whether the surface of the stone is smooth or rough, as well as upon its size, the inflammation will vary from a slight reddening of the mucosa to multiple areas of congestion and ulceration, producing bleeding. The stone may obstruct the urethral orifice and produce the usual vesical changes caused by back pressure, such as hypertrophy, trabeculation, and cellules; or its presence may aggravate already existing symptoms of back pressure caused by an enlarged prostate, stricture, or other obstruction. Obstructive and infective changes in the upper urinary tract are common complications of vesical stone.

Symptoms. Increased frequency of urination is usually the first symptom to be observed. Unlike the frequency of prostatic hypertrophy, which is generally more annoying at night, that induced by a vesical stone is likely to be worse in the daytime, when the patient is up and about. Other prominent but not pathognomonic symptoms are pain, hematuria (usually terminal), and sudden stoppage of the urinary stream. As a rule, the pain is most severe during or immediately following urination, but may be present at other times and is usually aggravated by motion. The character of the pain varies from a slight pricking to almost intolerable agony. In general, however, the pain due to a vesical stone is less severe than that produced by stone in the upper tract. It is most commonly felt toward the end of urination—in men being referred to the tip of the penis, and in women to the vulva. Occasionally, pain may be referred to the perineum, rectum, or even as high as the epigastrium.

Hematuria is a common but not invariable symptom. Most patients giving a history of hematuria will remark that the blood in the urine has been observed, as a rule, after violent exercise, heavy lifting, or prolonged jarring, such as may be experienced when horseback riding or during long motor trips. Such hematuria is usually painless. A large, rough calculus may traumatize the mucosa every time the bladder is emptied, so that each micturition will be terminated by a fresh show of blood.

Pus is almost always present in the urine, as a result of the accompanying cystitis, but may not be macroscopically evident.

Sometimes there are no symptoms suggestive of calculus, and the stone is only discovered at routine cystoscopy.

Diagnosis. A history of pain, sudden stoppage of the urinary stream, and hematuria, that is usually terminal and increased after exercise or prolonged motion, is suggestive of bladder calculus, and this suspicion will be increased if there have been attacks of renal colic prior to the onset of the urinary symptoms. Rectal or vaginal palpation may reveal the presence of stone in the bladder.

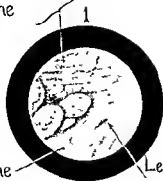
Suspected cases should be subjected to roentgenographic exploration. Many cases of bladder calculus can be diagnosed by plain films alone. However, reliance must never be placed on a negative x-ray film alone. Hyman, for example, has reported that in 35 of 57 cases of vesical calculus (61 per cent) no shadow was thrown by the stone. Calcified lymph glands in the vesical region may inject an element of confusion. In such cases, a lateral picture will show mobility of the shadow-casting bodies, and is an aid in the differential diagnosis.

The cystoscope is the urologist's main dependence in the diagnosis of vesical lithiasis (Plate VI). Uncomplicated bladder stone is rare, and cystoscopy will give full and accurate information not only regarding the stone but also as to the associated abnormalities, such as urethral stricture, prostatism, vesical diverticulum, and tumor. Calculi encysted in the bladder wall, or hidden away in a diverticulum (Fig. 238), may occasionally escape detection by even the most practiced eye, but the well-trained cystoscopist is not often thus led astray. Cystography and excretion urography are valuable aids to diagnosis even when used alone, but their worth is enhanced when reinforced by cystoscopy. A stone not opaque to the roentgen ray may readily be seen with the cystoscope.

Prognosis. With more exact methods of diagnosis, and greater surgical and manipulative skill, the outlook for most victims of vesical calculus can be regarded as excellent. For the patient enfeebled by age or intercurrent disease, the prognosis must be more guarded. This applies particularly to those postprostatectomy cases in which the patients are advanced in years and suffering from the effects of long-continued back pressure upon the upper urinary tract. The earlier vesical lithiasis is recognized and relieved, the better the prospect for permanent cure.

Treatment. Once formed, vesical stones that cannot be spontaneously expelled through the urethra must be removed by some form of surgery or intraurethral manipulation. Suprapubic lithotomy and litholapaxy are the methods in use today. Small stones may be removed with the cystoscopic rongeur. These procedures are discussed under Operative

Calculi behind
trigone

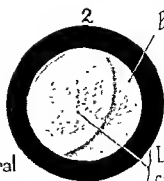


Trigone

Left ureteral
orifice

Wm P Diduch

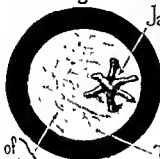
2



Bladder

Large
calculus

3

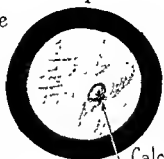


Jackstone

Orifice of
right ureter

Trigone

4



Calculus
arrested at orifice
of left ureter

5



Urine spurting from
distended ureterocele
on left side

6



Ureterocele collapsed
after discharge of urine

PLATE VI. CYSTOSCOPIC VIEWS

(1 to 4) Showing various types and locations of vesical calculi. (5, 6) Ureterocele, distended and collapsed.

Treatment of Vesical Calculus (p. 1124). Urinary antiseptics are often helpful in relieving the accompanying cystitis.

The value of dietetic treatment as an instrument of prevention will naturally be increasingly emphasized as the theory of vitamin deficiency as a causal factor in stone-formation gains ground. This phase of treatment is considered under Renal Calculus (Follow-Up Treatment; the Problem of Recurrence, p. 1609).

Foreign Bodies in the Bladder

The subject of foreign bodies in the bladder is intimately related to that of vesical calculus, because any extraneous object introduced into the bladder quickly becomes encrusted with urinary salts, and, if it is permitted to remain there for a considerable period, will form a nucleus for a bladder stone.

The list of foreign bodies which have been removed from the human bladder is an almost incredibly varied one. Among recent writers, Muller and Macquet offer a "certainly incomplete" list of 40 items beginning with *aiguilles* (needles) and ending with *vertèbres caudales d'un écureuil* (a squirrel's caudal vertebrae). They also describe the "astonishing bric-à-brac"—including a watch-chain and a crucifix—which Hogge removed at different times from the bladder of the same woman. In recent English reports is found an equally catholic selection, ranging all the way from the headless snake recovered by Geyerman, and the two snails which Mauterer found, to the match and fountain-pen cap recovered by McMartin. Anything that is not too large to be introduced into the urethra, or is capable of working its way through the tissues into the bladder cavity, or can be introduced and overlooked during vesical surgery, seems at one time or another to have played the part of foreign body in the bladder.

Etiology. Probably the greater number of objects are introduced by masturbators into the urethra, whence they escape during the engendered sexual excitement, so as to be beyond the reach of the introducer, whose frantic efforts to retrieve them only accelerate their passage into the bladder. Shame usually keeps the victim from seeking aid in their removal, as in most cases there are no immediate symptoms. The presence of the foreign body may actually be forgotten until the gradual encrustation of urinary salts so increases its bulk that a chronic cystitis is produced and, probably, an impediment to urination.

There appears to be a preponderance of females among the patients

on record as having introduced foreign bodies into the bladder for erotic purposes. Most of the females are young girls, who presumably have mistaken the urethral meatus for the vulva when attempting masturbation or the production of abortion.

Surgical accidents and material overlooked at operation are accountable for a small proportion of vesical foreign bodies. A broken-off fragment of catheter, filiform, lithotrite, or other instrument, a gauze sponge,

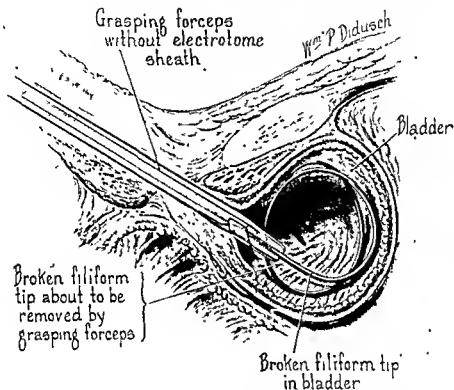


FIG. 237. A broken filiform tip in the bladder being removed with the Lowsley cystoscopic rongeur.

or a bit of drainage tube may be left behind in the bladder; and sutures have occasionally sloughed their way through the vesical wall, and, becoming encrusted, formed formidable stones.

Swallowed bodies, such as tacks, nails, needles, bits of glass, etc., have been recovered from the bladder, the introducers usually being young children or insane or intoxicated adults.

Bone spicules may work their way into the bladder from the extra-vesical tissues. Several authors mention the emptying of a dermoid cyst into the bladder, which may introduce teeth, hair, or even fetal

bones. Very rarely, fecal scybala invade the bladder through a vesico-enteric fistula.

The majority of the patients are young adults. We found no cases recorded in infancy, and few in old age.

Pathology. The bladder often tolerates the presence of a foreign body surprisingly well. Sometimes no symptoms are produced until the object becomes so encrusted with urinary salts that the resulting calculus almost fills the bladder. A smooth object, such as a prune pit or large glass bead, may remain in the bladder for a long time without becoming deeply encrusted or producing symptoms. Sharp-pointed objects, such as the ubiquitous hairpin of the earlier literature, are likely to become embedded in the vesical mucosa, rapidly setting up an irritation that is almost certain to become secondarily infected. Infection may have been present before the foreign body was introduced, or may have been carried in with it.

Occasionally an unusually rough or sharp-pointed article may perforate the bladder wall, forming a vesicovaginal or vesico-enteric fistula.

Symptoms and Diagnosis. In general, the symptoms of foreign body in the bladder are similar to those of vesical calculus. Depending upon the size and nature of the foreign object, and the condition of the bladder at the time of its introduction, distressing manifestations may supervene almost immediately or may be delayed for a considerable period. In many cases the victim will endure great torture before he will submit to examination, being ashamed or terrified of punishment if he admits his part in the introduction. The symptoms may be those of urinary blockage, cystitis, or both.

The diagnosis is easily made if a correct history can be obtained. This, however, is usually difficult. As with vesical calculus, the diagnosis is based upon the history, rectal or vaginal palpation, and the cystoscopic and roentgenographic findings.

Treatment. The methods of treatment suggested for bladder stone are applicable to foreign bodies (*Operative Treatment of Vesical Calculus and Foreign Bodies in the Bladder*, p. 1124).

Numerous instances are on record wherein portions of paraffin or wax in the bladder have been dissolved by various solvents (xylol; one-third gasoline in warm paraffin oil; warm, sterile liquid petrolatum, etc.). Solvents such as chloroform, benzine, and carbon disulfate ether cannot, of course, be used in the bladder. The best method, in our opinion, is to remove the paraffin, piece by piece, with a cystoscopic rongeur.

Vesical Fistulas

VESICOVAGINAL FISTULA

A fistulous communication between the bladder and the vagina is a relatively common and an exceedingly distressing lesion, the successful repair of which presents a most difficult problem. Until a comparatively few years ago cure was almost unheard of; and any extensive series of cases, such as that published by us from the records of the New York Hospital from 1844 to 1933, was invariably made up largely of tragic failures. The first successful technic was that devised by Marion Sims in 1852—an operation which ranks with the great surgical achievements of all time, and which, with certain modifications, is still applicable to patients of the present day.

Etiology and Pathology. The proximity of the female bladder to the vagina makes an accidental opening between these two hollow structures an ever-present possibility. Most of the vesicovaginal fistulas reported in the earlier literature were the results of accidental obstetrical injuries. In later years we find them frequently following pelvic operations, especially hysterectomy, radium treatment of the genital canal, or neoplastic or inflammatory disease of the cervix, vagina, or bladder.

The vaginal orifice of the fistula is regularly located in the upper half of the anterior wall. The size of the orifice may vary from that of a pin-head to so great a loss of substance that the examiner can easily thrust several fingertips through it. In fistulas of long standing there may be inversion of the vesical mucosa through the orifice and a dense ring of scar tissue encircling it.

The constant leakage of urine through the opening creates a distressing condition and renders the lives of these women most miserable. Often the mucous membrane about the fistulous opening shows an inflammatory reaction from the constant irritation, especially if the patient is suffering from cystitis. *Decomposition of urine results in deposits of ammonium salts about the edges of the fistulous opening.* When the fistula is due to radium injury, the floor of the bladder is likely to show extensive sloughing, with dense scar tissue, and there may be wide loss of substance in both the bladder floor and vaginal vault.

Symptoms and Diagnosis. Urinary incontinence is the chief symptom. A history of difficult labor, a pelvic operation, or radium therapy preceding the onset of the incontinence is important. The vaginal speculum will usually reveal the vaginal orifice, with urine leaking

through it as a rule; and cystoscopy may show the vesical opening, which is likely to be found in the midline, posterior to, or near, the interureteral ridge. Very small openings may be disclosed with the aid of cystography or the intravesical or intravenous injection of methylene blue.

Prognosis. The prognosis of vesicovaginal fistula, once uniformly poor, has been so improved by modern surgery that successful closure may be hoped for in the majority of cases.

Treatment. Very small vesicovaginal fistulas of traumatic origin, if immediately recognized and the urine promptly diverted, may heal spontaneously. Usually, however, surgical closure is required (Repair of Vesicovaginal Fistula, p. 1128).

VESICO-ENTERIC FISTULA

A fistulous communication between the bladder and the bowel is not rare. It is seen more often in the male sex. The opening may be between the bladder and the rectum (the most common variety), sigmoid, ilium, or appendix. Pascal (1900) collected 346 cases from the literature, and called attention to the predominance of male patients, placing the ratio at 3 males to 1 female. Cunningham (1916) exactly reversed this ratio, claiming that 75 per cent of vesico-enteric fistulas were seen in women and only 25 per cent in men. In Higgins' report of 35 cases seen at the Cleveland Clinic (1936), 21 were males and 14 females. This author remarks that the greater incidence in men may be accounted for by the fact that men are more subject to diverticulosis than women. Communication between the bladder and bowel is anatomically more difficult in the female because of the interposition of the uterus.

Etiology. The cause of the fistula may arise in the bowel, in the bladder, or outside both. External trauma (gunshot wounds, etc.), surgical accidents, and inflammatory or neoplastic disease of the bladder or intestine are the most common causes. Diverticulosis of the rectum or sigmoid is responsible for many of these fistulas. Occasionally a stone or foreign body becomes embedded in the portion of the vesical wall impinging on the lower bowel, and, by eroding through, eventually produces a fistula. Abscess-formation in a similar location may have a like effect. A few cases are of congenital origin, accompanying imperforate anus.

Pathology. The communication is generally directly through the apposed vesical and intestinal walls; but occasionally there is a long, tor-

tuous tract between the bowel and the bladder, such a sinus being usually due to the burrowing of pus from an extravescical inflammatory process.

The location of the vesical opening depends upon the causal factor. In cancer of the rectum the opening is usually found on the left wall.

Symptoms. Diverticulitis, to which many vesico-enteric fistulas can be traced, may produce vesical symptoms before the fistula is actually established. If the sacculation in the intestinal wall impinges directly upon the bladder, there will be pronounced vesical symptoms: a burning sensation in the affected portion of the bladder wall, tenesmus, and the less characteristic symptoms of frequency and urgency.

As soon as an opening between the bladder and the bowel has been established, an acute cystitis is usually set up. There will then be distressing frequency and urgency, pyuria, and sometimes hematuria. The pathognomonic symptoms are the passage of gas and feces in the urine, the amount depending upon the size and location of the opening into the bladder. If, however, the communication is very small, or there is considerable edema about the fistulous opening in either the bowel or the bladder, the size of the orifice may prevent the passage of fecal particles into the urine, so that this sign will be lacking. Sometimes the urine leaks into the bowel, resulting in watery stools.

Diagnosis. The passage of flatus and bowel contents in the urine, or of urine in the bowel contents, is usually sufficient to establish the diagnosis, which is confirmed by cystoscopy, cystography, and examination of the rectum.

Cystoscopy will usually reveal the location of the vesical opening of the fistula. The accompanying cystitis may be widely disseminated throughout the bladder, or the inflammatory changes may be localized in a circular, intensely red spot at the site of the fistulous communication. Differentiation from bladder tumor may at times be difficult, because adherence of the neoplastic or inflammatory intestinal mass to the bladder wall will produce a localized area of edema with mucosal projections which closely simulate the fronds of vesical papilloma. The edema may completely conceal the fistulous opening. If the cystitis is diffused, investigation of the upper urinary tract is indicated.

Cystography will disclose the location, extent, and direction of the fistula.

Proctoscopy or digital examination will reveal the bowel opening if it is located low enough. If located higher up, roentgen examination after barium enemas may be necessary to locate the intestinal opening.

Prognosis. Without operative intervention the prognosis is grave, because of the ascending colon-bacillus infection of the upper urinary tract that is sure to follow this condition.

If the fistula is of the type that can be controlled by the institution of a colostomy, the prognosis is excellent; but in extensive rectal or vesical carcinoma the prognosis is very grave and is dependent upon that of the malignant lesion.

Treatment. The treatment of vesico-enteric fistula will differ with the type, but is always surgical. Operative relief is indicated as soon as the diagnosis is established, if the patient's condition warrants the procedure.

A fistula incurred during surgical intervention may heal spontaneously if prompt bladder drainage, by suprapubic cystostomy or a retention catheter, is instituted. Other fistulas, if not too extensive, and, particularly, if associated with diverticulosis, may heal spontaneously if the fecal current is diverted by a colostomy. In most cases, however, laparotomy is necessary, to separate the adherent bladder and bowel and repair the openings in the walls of both organs.

Fistulas secondary to carcinoma of the bowel may be inoperable or relieved only by a permanent colostomy. A few patients have been subjected to cystectomy and ureteral implantation preceded by transection of the bowel, removal of the malignant area, and closure by end-to-end anastomosis. The wisdom of subjecting an elderly patient to such an extensive surgical intervention is questionable.

VESICO-UTERINE FISTULA

Etiology and Pathology. Vesico-uterine fistulas, like those between the bladder and vagina, are the result of accidental obstetrical, gynecological, or urological injury, radium therapy, or inflammatory or neoplastic disease of the bladder or uterus. They are not common. This type of fistula is most often incurred during labor, from the pressure of the presenting head above the superior strait. If the head is uncommonly large or misshapen, it may lacerate or devitalize the tissues, with subsequent necrosis and sloughing. Anterior lacerations of the cervix, occurring directly in the median line and extending into the bladder, are the injuries most frequently observed.

Symptoms and Diagnosis. The symptoms are similar to those of vesicovaginal fistula, leakage of urine from the vagina being the most prominent complaint. If the fistula has been in existence for some time

when the patient presents herself for treatment, there may be evidences of partial spontaneous healing. Granulations may have partially closed the lacerations at the bladder base, or even entirely filled the opening in the uterine cervix. Occasionally most of the laceration will be found bridged over, with only a small fistulous tract remaining, usually at the bottom of the original fissure. But even through these contracted openings the urine will flow into the uterus and leak down into the vagina, being visible as soon as the speculum is inserted.

The diagnosis is made by cystoscopy and cystography. The appearance in the uterine os of methylene blue injected into the bladder is definite evidence of a communication between the two organs.

Prognosis. Except in those cases due to malignant disease, or accompanied by very extensive loss of tissue, the chances of successful operative repair are good.

Treatment. The treatment of choice is to close each fistula separately, making sure that the suture lines do not come in contact with each other. If many adhesions have formed, there may be great difficulty in dissecting the cervix free from the bladder wall. In women near the menopause, vaginal hysterectomy may offer the most satisfactory solution. As with vesicovaginal fistula, cystectomy with transplantation of the ureters into the bowel has been suggested for very obstinate cases, when all efforts at closure have failed.

Diverticulum of the Bladder

Vesical diverticulum is an evagination or herniation of a portion of the bladder wall, producing a sac with a narrow neck. The diverticulum may vary in size from a small cellule 1 cm. in diameter to a sac larger than the bladder itself. The opening into the diverticulum is always much smaller than the sac itself, and from the interior of the bladder has the appearance of an orifice. The diverticulum acts as an accessory urinary reservoir which does not empty with the bladder at the first urination. When patients complain, as they frequently do, of being able to void an equal amount shortly after emptying the bladder, diverticulum is immediately suspected. Numerous instances of calculi or tumor occurring in a diverticulum have been reported.

For a résumé of the literature on this interesting lesion, to which physicians from the time of Hippocrates down to the present have been calling attention, the reader is referred to the very complete history published by Lowsley and Gutierrez in 1928.

Incidence. The frequency of vesical diverticulum is now known to be much greater than was formerly supposed. Prior to the practical use of the x-ray and cystoscope, relatively few reports of diverticulum of the bladder appeared in the literature, and these were generally postmortem or unsuspected operative findings.



FIG. 238. Diverticula of the bladder. (a) A large collection of small bullet-like calculi in a diverticulum. (b) A smaller sac higher up on the bladder contained no stones. This patient was entirely cured by operative intervention.

Diverticulum is much more common in males than in females (18 females to 543 males, Schacht and Crenshaw, 1930). It may occur at any age; but is uncommon in childhood, occurs chiefly after the fourth decade, and is most common in later years. Indeed, the preponderance of men of "prostatic age" is too striking not to be significant.

Etiology. The etiology of vesical diverticulum has been widely studied and extensively investigated during recent years. The general conclusion is that the condition is the result of both congenital and acquired factors; that it cannot be attributed to any one etiological factor, but is

the result of a number of causes—anatomical, pathological, and mechanical—operating together, so that, even if some congenital defect may have contributed toward its formation, in the vast majority of cases the diverticulum may properly be considered as an acquired lesion.

By far the most frequent sites of diverticula are in the region of the ureteral orifices on the posterior or lateral wall, and at the site of the urachus. Although congenitally weak spots in these parts of the bladder wall are undoubtedly a predisposing factor, it is doubtful if diverticulation occurs unless there is obstruction. In the presence of long-standing back pressure, it is these weak points in the wall that are most likely to give way. Accessory ureteral buds and patent urachi explain a few diverticula, but here, too, obstruction is probably always an accessory factor.

Ernest M. Watson, in his investigations of the fetal bladder in various stages of development, observed that, in the fetus, intrapelvic and lower abdominal pressure often varied considerably, and that this resulted in distortion of the bladder, causing irregularity of the inner wall with ridge-like elevations about the lateral margin of the trigone. If pressure should become great enough early in fetal life, these ridges might possibly develop to such an extent as to bridge the lumen of the bladder, for in some of the specimens studied by Watson the irregular ridges traversed the entire vesical cavity, so as to touch the mucosa of the opposite wall. Lateral pressure might cause the formation of similar bridges from one part to another of the same side of the bladder. There were indications that if destruction of the epithelium should take place, and two surfaces thus denuded come together, conditions would be favorable for their adherence, thus forming a true attachment of the bridge of tissue across some portion of the vesical cavity. As the mucosa continued to grow, it would send out finger-like projections which eventually would grow into a continuous wall until, finally, a true pocket, containing all the elements of the bladder wall proper, would be formed.

It is probable that many congenital diverticula remain unrecognized throughout life, and that many others produce no symptoms until after middle life, when factors inducing abnormal intravesical tension, or increased activity of the vesical mucosa, may bring pressure to bear upon the weak points in the wall.

The role of lower urinary-tract obstruction is of outstanding importance in the production of vesical diverticula. Urethral stricture, congenital valves, prostatic hypertrophy or carcinoma, contracture of the

vesical neck, and bars are the lesions chiefly responsible. Paralysis, with retention of urine, may result in the formation of diverticula. The obstructed bladder, attempting to empty itself, forms trabeculations, and then shallow cellulcs (Plate VII). If the urinary back pressure continues, one or more of these cellulcs may increase greatly in size, forming a diverticulum. The much greater incidence of obstruction in men than in women accounts for the striking predominance of diverticulum in the male sex.

Pathology. Diverticula may be small or of great size, single or multiple, simple or multilocular. In approximately 50 per cent of our cases the diverticula have been multiple. The wall of the sac consists largely of connective tissue, being deficient in muscular fibers. The sac is lined with vesical mucosa. Most diverticula are non-contractile, due to the inelasticity of the wall and adhesions to surrounding structures. Infection of the retained urine often leads to diverticulitis, ulceration, calculus, or (infrequently) tumor.

Symptoms. The symptoms are many and varied, being chiefly those of obstruction of the urinary tract: increased frequency of urination, a slow, sluggish stream, dribbling, hematuria, pyuria. Suprapubic pain, or a sense of fulness or pressure in the lower abdomen, or burning during or after micturition may occur. A history of having to empty the bladder twice in rapid succession is characteristic of this condition. The urine is usually foul, due to stasis.

In most cases the symptoms have been present for a long time when the patient seeks medical aid (an average of $5\frac{1}{2}$ years in our series).

Diagnosis. The diagnosis is made upon the history and by cystoscopy and contrast cystography.

The few diverticula encountered in children practically always are found in boys, and are usually accompanied by congenital valves, spina bifida, or some other cause of obstruction. The condition is uncommon in women. Most of the cases occur in older men, and are accompanied by some condition of prostatism, median bar, or urethral obstruction. In making the diagnosis, therefore, it is not enough to establish the presence and size of the diverticulum; the causative lesion in the lower urinary tract, and complications in the bladder or in the upper tract, must also be investigated and accurately diagnosed.

Cystoscopy reveals the location of the orifice of the diverticulum. An x-ray-opaque ureteral catheter may be passed into the cavity of the diverticulum, where it will curl up, and an x-ray will show its location.

The best method of diagnosis is the cystogram followed by an aerogram. Radiograms are first taken with the bladder and diverticulum filled with an opaque fluid; the opaque medium is then removed, the bladder immediately filled with air, and another radiogram taken. When the diverticulum is retentive, the opaque fluid will be found to be retained in the sac.

Prognosis. The prognosis is largely dependent upon the extent of damage to the upper urinary tract and bladder by back pressure and infection. If the damage to the kidneys is not too great, the prognosis is usually good, following removal of the obstructive cause of the diverticulum, and of the diverticulum itself if it is retentive.

Treatment. Non-retentive diverticula do not require surgical removal. In these cases, removal of the obstructive cause of the diverticulum and frequent vesical irrigations are indicated.

Retentive diverticula, occurring at any age, should be surgically removed by the one, two, or three-stage operation, as indicated. Preliminary drainage of the bladder, as a precursor to diverticulectomy, is just as essential as it is for prostatectomy. Removal of any existing obstruction in the lower tract is also necessary (Resection of Vesical Diverticulum, p. 1111).

Neurogenic Abnormalities of the Bladder

The relation between disturbances of the bladder and lesions of the central nervous system and peripheral innervation has of late years been the subject of extended investigation by both neurologists and urologists. There are many phases of the subject, however, that still require clarification. In urological practice, the important point is to recognize that a particular disturbance of urination is caused by a lesion of the nervous system, since the treatment of these cases differs greatly from that of vesical dysfunction due to mechanical obstruction or infection—although it must be remembered that neurogenic, obstructive, and infectious lesions may all be present in the same bladder. It is a fairly prevalent custom, even today, to classify as “neurotics” and “neurasthenics” patients who complain of more or less constant bladder symptoms in spite of negative cystoscopic findings and a normal urinalysis. While undoubtedly an occasional case of so-called neurosis of the bladder is basically neurasthenic, in many instances a careful neuro-urological investigation would probably reveal a definite lesion of the nervous system as the responsible factor in the production of the vesical symptoms.

Lesions of the Nervous System Producing Vesical Dysfunction.

Lesions of the central nervous system that often cause disturbances of bladder function are: traumatic injuries to the brain and spinal cord; cerebral or spinal tumors; diseases of the brain or cord, such as general paresis, tabes dorsalis, syphilitic spinal paralysis, multiple sclerosis, ataxic paraplegia, transverse myelitis, poliomyelitis, arteriosclerosis of the cord, spina bifida, and lesions of the cauda equina.

Lesions of the peripheral nerves producing disturbances of urination are of four types: (1) congenital, (2) inflammatory, (3) mechanical, (4) indeterminate.

Of congenital lesions, spina bifida is the most common. In spina bifida occulta the effect upon bladder function may be the only outward evidence of the spinal abnormality. In the absence of interference with defecation, or of somatic alterations, the defect is usually assumed to be in the peripheral innervation of the bladder, most likely directly in the vesical plexus. Retention, with eventual overflow incontinence, is the usual clinical picture.

Inflammatory involvement of the peripheral nerves may occur in the course of diabetes or infectious fevers such as scarlet fever, diphtheria, or pneumonia, or be part of an alcoholic neuritis. Peripheral neuritis produces urinary frequency and urgency, but rarely actual retention. Because the symptoms of these lesions resemble those of infection, and the irritative phase is likely to be transitory, inflammatory lesions of the peripheral nerves are not often described in the literature.

A number of mechanical factors may cause injury to the peripheral nerves of the bladder: pressure upon the nerves by the fetal head during labor, or from a retroflexed gravid uterus during pregnancy, or by an extravescical tumor; direct surgical injury to the nerves during an operation upon neighboring structures; and spondylolisthesis. Several decades ago Spiller described how enuresis could be induced by forceful stretching of the sacral nerve roots while in the sitting position.

Indeterminate factors include vaguely understood lesions of the peripheral nerves resulting in various degrees of incontinence or retention.

Clinical Types of Neurogenic Vesical Dysfunction. Irrespective of whether the nerve lesion is central or peripheral, the gross manifestations in the bladder are varying degrees of retention and incontinence. Of clinical importance are (1) the paralytic bladder, (2) cord bladder, (3) atonic bladder, due to lesions of the peripheral nerves, (4) hypertonic bladder.

Paralytic Bladder. Paralysis of the bladder follows injury to the spine. The injury may be as low down as the lumbar region, including trauma of the cauda equina. There is complete inability to empty the bladder, resulting in hyperdistention, with great pain. Overflow incontinence follows, but the bladder remains distended.

Gordon Holmes (1933), in his studies of the paralyzed bladders of men who had suffered complete transverse lesions of the spinal cord during the World War, noted that immediately after a complete transverse lesion of the cord at any level, or of the cauda equina, the bladder acts merely as an elastic reservoir and gives no evidence of nervous control. Subsequently, however, the bladder wall regains its muscle tonus to a certain extent, so that eventually the bladder again becomes actively reflex, at least in those cases where the injury is above the sacral segments of the cord.

More recently (1937) Thomson-Walker has expressed the same opinion: that destruction of the supralumbar or lumbar portions of the cord, or of the cauda equina, is followed by (1) a stage of retention and (2) a stage of periodic reflex micturition. The average duration of the first stage, he found, was about 55 days; and during this stage, after some hours or days, the urine begins to dribble away, the bladder remaining distended. The second stage develops gradually, and the periodic reflex contractions increase in strength until the bladder is able to empty itself completely.

The diagnosis of paralytic bladder is made on the history.

Cord Bladder. Cord bladder is the type of vesical dysfunction commonly seen in lesions of the central nervous system. The predominant symptom is retention. There is often frequency of urination, but very little discomfort.

The cord bladder, whether due to a syphilitic or other spinal cord lesion, is characterized by general relaxation of the bladder wall, generalized faint trabeculations of the mucosa, relaxation of the internal sphincter with hypertonicity of the external sphincter, and anesthesia of the posterior urethra and vesical neck. Typical of the cystoscopic picture is the complete relaxation and dilatation of the vesical neck, so that the posterior urethra has the appearance of being a part of the bladder. If, during cystoscopy, the ordinary Brown-Buerger cystoscope can be withdrawn into the posterior urethra and the verumontanum observed, without signs of distress or protest from the patient, a tabetic bladder should be suspected. In tabes, the vesical signs and symptoms are

often the first manifestations of the nervous lesion, and may appear long before the disturbances of pupillary reflexes and knee jerks. Therefore, with the aid of the cystoscope, the urologist may often make a diagnosis far in advance of the neurologist.

The diagnosis of cord bladder is usually not difficult unless mechanical obstruction of the vesical neck is also present. The diagnosis is made on the history and by cystoscopy, cystography, and cystometry. Examination of the spinal fluid proves the presence of tabes.

Atonic Bladder. The atonic bladder due to various lesions of the peripheral nerves is of clinical interest chiefly in relation to spina bifida occulta and vesical dysfunction in children. Braasch (1925) described two types of atonic bladder of neurogenic origin: (1) the large, relaxed bladder due to interference with the motor fibers alone, with rather pale and smooth mucosa, thread-like trabeculations, no relaxation of the internal sphincter, and little or no loss of sensation; (2) the atonic bladder due to disturbances of both motor and sensory fibers, which may give a picture difficult to distinguish from cord bladder. The first type is usually readily differentiated cystoscopically and by cystogram, and the cystometrogram will show definite absence of tone of the detrusor muscle. With this type of bladder there is generally definite clinical evidence of some neurological lesion. As a rule, sensation in such a bladder is normal or nearly so, but control is imperfect, resulting in retention, incontinence, and enuresis.

Hypertonic Bladder. By hypertonic bladder is meant a condition where an urgent desire to urinate is felt when the bladder contains no more than 150 cc. of urine, and involuntary urination takes place if the bladder content is not immediately evacuated.

Diagnosis of Neurogenic Abnormalities of the Bladder. The diagnosis of paralytic, cord, atonic, and hypertonic bladders is based on the findings of cystoscopy, cystography, and cystometry. Dysfunction of neurogenic origin must be differentiated from that due to obstruction.

Prognosis. The outlook for the patient whose bladder is paralyzed as the result of trauma is not a bright one. Traumatic injuries to the cord are always grave, and even when the vesical nerves partly regain their tone, the hope of permanent recovery of function is not great. The prognosis of paralysis or atony due to syphilitic or other disease of the central nervous system is bound up with that of the nervous lesion. Antiluetic treatment has produced excellent results in some cases of

tabetic bladder. *Automatic bladder* is frequently established in complete transverse lesions of the cord, but never in incomplete cord lesions and peripheral involvement. Under any circumstances, the necessity of practicing artificial emptying of the bladder over a long period inevitably results in urinary-tract infection, so that, in the last analysis, the prognosis depends largely upon the extent of urosepsis. Recent advances in the diagnosis and therapy of vesical dysfunction of neurogenic origin offer a somewhat more hopeful outlook for the future.

Treatment. In all types of neurogenic bladder, catheterization should be avoided by every means possible because of the infection that is bound to follow.

Most paralytic bladders due to trauma will satisfactorily establish an overflow incontinence, and, if infection can be avoided, periodic reflex micturition may eventually develop. Early suprapubic cystostomy gives relief from the agonizing pain of many of these cases, without interfering with the development of automatic function. The success of these measures depends upon the extent of the primary nerve injury and the promptness with which relief measures are instituted.

The treatment of cord and atonic bladders is secondary to that of the lesion in the central nervous system and peripheral nerves. No permanent improvement can be looked for unless the cause can be removed. This often presents a fine problem in neurosurgery. Syphilis, diabetes, and pernicious anemia, all of which may produce neurogenic bladder, must have appropriate treatment. The treatment of the bladder consists largely in combating the inevitable urinary infection and the frequent formation of calculi. The pH of the urine can usually be controlled by appropriate drugs and diet. Permanent suprapubic cystostomy, with vesical irrigations through the tube, is often advisable. Some success has been reported with mecholyl and other drugs which act as parasympathetic stimulators. Urinary antiseptics should be regularly employed. In selected cases of cord bladder, presacral neurectomy has given excellent results in several of our cases, relieving the residual urine entirely and lessening the urinary infection.

Enuresis

Most dictionaries define *enuresis* simply as "the involuntary discharge of urine," but in urological practice the meaning of the term is generally confined to the common bed-wetting difficulties of early childhood, in contradistinction to the true urinary *incontinence* seen in adults suffering

from neurogenic disturbances, the after-effects of operative procedures, etc., and in children with congenital abnormalities such as exstrophy of the bladder, epispadias, and valves of the posterior urethra. While enuresis in the great majority of cases can be relieved by the establishment of proper habits and environment, incontinence usually requires resort to surgery, and, because of its more serious character, is much less favorable in its prognosis.

Enuresis, particularly the nocturnal variety, is not to be regarded as abnormal up to the age of 3 years. Usually, by the end of the first year of life the child has begun to acquire voluntary control of the bladder function, at least during the daytime. By the end of the second year most children have gained complete urinary control, and any child who still has involuntary urination when he has reached 3 years of age, may properly be said to suffer from enuresis. Functional enuresis is not, therefore, a disease but simply the persistence of an infantile condition or habit.

Etiology. The cause of this persistence, in many cases, can never be satisfactorily determined. Frequently, of course, it is due to failure of parents or attendants to establish habits of bladder control in the first year or so of life. It has frequently been observed that many children presenting this condition are exceedingly active and nervous, and often do not get enough rest to counteract the strain of a long and active day. It is possible that general bodily fatigue may be responsible for the prolongation of the enuresis in these cases. In the Navy, where men are required to sleep on their backs in hammocks, there are found a certain number of adult cases of enuresis.

Psychic factors loom large in the opinion of many pediatricians, as well as other observers, both lay and medical. Campbell claims that enuresis is much more common in institutional children than in those from normal private homes. He also observes that the child usually "directs his enuresis towards his mother"—that is, he uses it as a device to obtain maternal attention. This experienced urological pediatrician advocates the father taking the mother's place in ministering to bed-wetters (waking in the night, etc.) so that this fixation upon the mother may be broken up. There is no doubt that in many cases a wrong attitude on the part of one or both parents may have strong etiological bearing.

In many cases, enuresis results from some definite local abnormality requiring correction: phimosis, redundant prepuce, adherent clitoris,

congenital narrowing of the meatus, anal fissure, vaginitis, etc. The more serious congenital urological and neurogenic lesions are discussed elsewhere. Malnutrition, diabetes, and naso-pharyngeal obstruction may also be responsible. Cystitis and pyelitis should be ruled out. Excessive acidity or alkalinity of the urine may promote vesical irritability which will lead to involuntary evacuation of the bladder even when it contains but a small amount of urine. Both boys and girls have been found to have congenital stricture of the bladder neck, with an effect upon the upper urinary tract not unlike that seen in elderly prostatics. Children thus afflicted are subject to overflow incontinence not recognized as due to retention.

Butterfield (1930) states that he has encountered numerous cases of nocturnal incontinence, and occasional cases of frequent urination, all with clear and uninfected urines, which failed to respond to the usual methods of treatment; and that in every instance in which cystoscopy was permitted, definite changes at the bladder neck (thickening, infiltration, cystic masses), with varying amounts of residual urine, were found. This emphasizes the importance of investigation of the child's vesical orifice and urethra in obstinate cases of enuresis; and with the Butterfield baby cysto-urethroscope (p. 89), such investigation, as well as treatment of the condition, may readily be done, even in very young infants. In many instances the mere passing of the cystoscope, by dilating the orifice, results in a clearing up of the irritation; in others, fulguration or other treatment is necessary.

Symptoms and Diagnosis. The only invariable symptom is the involuntary discharge of urine, usually during sleep. All young bed-wetters are very sound sleepers and not only fail to wake during the urinary act but sleep in wet clothing as well. Sometimes the child is of a neurotic type, but just as often enuresis is found in otherwise normal children who display no nervous symptoms or emotional instability. If the enuresis is due to an organic lesion, other symptoms common to the particular ailment may be present.

A thorough examination is necessary to rule out all possible causes of unusual frequency and involuntary micturition—systemic, neurological, and urological.

Prognosis. In young children, the prognosis is usually good, if vigorous measures are used, and if there is no serious physical abnormality or mental deficiency. In older patients, the results of treatment are less certain, particularly if the habit has persisted over many years and

if there are present urinary-tract abnormalities which have produced extensive impairment of renal function. Even after removal of the organic lesion, the enuresis may persist as a habit.

Treatment. If a local organic cause for the incontinence is found, this, of course, must be removed.

Cases of functional enuresis in children are most successfully handled by the establishment of proper habits. Never punish a child for wetting his bed; rather, praise and reward him when he succeeds in getting through the night dry. The child should be sent to the toilet at frequent intervals during the day and just before retiring, and awakened during the night *before* the accustomed time of bed-wetting. He should be prevented from lying on his back by having a knotted towel tied about him. Fluids should be withheld after the evening meal, which should be a light one. The establishing of regular habits, in combination with careful attention to diet, and the abolition of fatiguing and exciting factors in the child's mental and physical life, will usually serve to correct most cases of functional enuresis.

If all measures fail, hospitalization of the child for a week or two will sometimes accomplish the desired cure by its psychic effect.

Incontinence of Urine

True incontinence of urine is seen in children in association with congenital malformations, such as exstrophy of the bladder, epispadias, extravescical ureter, and patent urachus, and in malformations of the nervous system, such as spinal bifida.

In the adult, aside from the cases of infantile enuresis which have been permitted to persist into adult life, there is a distinct group in whom the inability to control the urine is due to other causes—congenital or acquired. These have been grouped by Farman as follows: (1) *urethral*: urethrocele, stricture, diverticulum, tumor, caruncle, paresis of sphincter, trauma to urethral sphincters, incomplete union of voluntary and involuntary fibers of sphincter (nullipara); (2) *vesical*: tumors, tuberculosis, advanced cystitis (interstitial), relaxation of vesical wall due to childbirth (a) total disruption of tissues—*fistula*, (b) alteration of tissues and vesical sphincter (partial or complete incontinence), cystocele, mechanical occlusion of vesical outlet (overflow incontinence); (3) *gynecologic-obstetrical*: injury at childbirth, injury during gynecological surgery, fibroid (compression of bladder), ptosis of uterus, *vesicovaginal fistula*, *urethrovaginal fistula*, *ureterovaginal fistula*, *symphysiotomy*; (4) *nervous system*: de-

fective innervation of the sphincters, meningo-vascular syphilis—irritative type, tabes dorsalis—destructive type, spinal cord tumor or injury, neurogenic bladder (a) supranuclear lesions, (b) nuclear and infranuclear lesions; (5) *systemic causes*: hysteria, neurasthenia, severe toxic state, highly acid urine (urgency rather than true incontinence). Most of these factors have already been considered.

In the female, a relaxed vesical sphincter is a not infrequent cause of incontinence in women who have borne children, especially those who have undergone difficult instrumental labors. This incontinence may appear immediately after delivery, or several years may elapse before urinary control is lost. When seen in women who have neither borne children nor undergone an abdominal operation, it must be attributed to nervous disturbance or progressive muscular weakness.

It is most important that the cause of the incontinence be determined with certainty before surgical correction is undertaken. Incontinence arising from disease of the central nervous system, for example, is seldom amenable to surgical correction.

The operative treatment of urinary incontinence is discussed under Operative Treatment of the Bladder (p. 1137).

Lesions of the Urinary Bladder in Children

Cystitis is the most common vesical abnormality encountered in children, and is invariably an accompaniment of upper urinary-tract infection. The most important part of the treatment is the elimination of the extravesical source of infection. Locally, the bladder is treated in much the same manner as in adults.

Exstrophy of the bladder is best repaired in early youth, to prevent the probability of cancer of the abnormal bladder and the fatal infection of the urinary tract which sometimes results from ureteral transplantations in adults, but rarely in children.

Vesical stone has become a rare lesion in the United States and most European countries, although it is common in India and certain other regions. Suprapubic lithotomy is the treatment of choice when the patient is a child.

Diverticulum of the bladder is rare in children.

Incontinence due to spinal bifida may be relieved by the method developed by Lowsley and described on page 1137.

Bladder tumors are rarely encountered in children. A review of the literature by Deming, in 1924, revealed only 64 authentic cases seen in

the first decade of life. Rathbun (1937) collected 75 cases, which he tabulated as follows:

	<i>cases</i>
Sarcoma	38
Myxoma	16
Myxosarcoma	4
Neurogenic sarcoma	1
Fibroma	5
Fibromyoma	1
Neurofibroma	1
Myoma	1
Rhabdomyoma	2
Polyps (benign)	2
Dermoid	1
Papilloma	1
Hemangioma	2
	<hr/> 75

Tumors in children are regularly mesothelial in nature, epithelial growths being almost unknown. Not only are sarcomas the most common; they are also the most intensely malignant. They may be observed at any age, but occur most frequently before the fifth year. The prognosis, even when the tumors are seen early, is uniformly poor.

As is the case with adult patients, the symptoms of bladder tumor in children are few and frequently misleading. The most common symptom is painless hematuria. This, however, may not occur until late, since blood usually enters the urine only after ulceration has taken place, and mesothelial tumors are slow to ulcerate. Urinary difficulties consist of frequency, urgency, tenesmus, incontinence, and, if the tumor grows rapidly or is located near the internal sphincter, retention. The papillomas of adult bladders produce greater suffering than the mesothelial growths seen in infants and young children; but in trigonal growths the pain may be very severe, being usually referred to the lower part of the abdomen.

Most vesical neoplasms seen in children run a rapidly fatal course no matter what the treatment employed. Even the histologically benign growths may prove fatal because of their location or the complications which they induce. In general, remedial measures for the rare bladder tumors of childhood follow along the same lines as those employed in adult patients. The small caliber of the child's urethra makes transurethral maneuvers difficult; therefore open operation will be found more desirable.

BIBLIOGRAPHY

- ALBRIGHT, F., *et al.*: Studies in parathyroid physiology: effect of phosphatic ingestion in clinical hyperparathyroidism. *J. Clin. Investigation*, 11: 411, 1932.
- ALLEN, A. B.: Gangrene of the bladder. *Urol & Cutan. Rev.*, 40: 629, 1936.
- APPERMANN, E.: Malakoplakia of the bladder. *Ztschr. f. Urolog*, 18: 164, 1924.
- ASCHER, P. W.: Clinical applications of tumor pathology. *Surg, Gynec, Obst.*, 52: 979, 1931.
- ASH, E. J.: Epithelial tumors of the bladder. *J. Urol*, 44: 135, 1940.
- BACON, L. H. AND LECOUNT, E. R.: (Rupture of the bladder). Automobile injuries: study from records of postmortem examinations. *Arch. Surg.*, 18: 769, 1929.
- BARRINGER, B. S.: Carcinoma of the bladder. *Surg, Gynec, Obst.*, 57: 867, 1934.
- BEARD, J. W., *et al.*: The nature of a virus associated with carcinoma in rabbits. *Surg., Gynec. & Obst.*, 74: 509, 1942.
- BEER, EDWIN: Removal of neoplasms of the urinary bladder, a new method, etc. *J. A. M. A.*, 54: 1768, 1910.
- BEER, EDWIN: Bladder tumors: diagnosis and treatment. *Surg. Clin. N. America*, 13: 255, 1933.
- BEGG, R. C.: The colloid adenocarcinomata of the bladder vault arising from the epithelium of the urachal canal. *British J. Surg*, 18: 423, 1931.
- BLASUCCI, M. D.: Calculus in the female bladder 12 years after repair of vesicovaginal fistula. *J. Urol*, 35: 652, 1936.
- BOND, STERLING: Foreign bodies in the bladder. *J. A. M. A.*, 83: 1163, 1924.
- BOUN, H. K.: Hernia of the urinary bladder. *Urol. & Cutan. Rev.*, 40: 484, 1936.
- BRAASCH, W. F., AND THOMPSON, G. J.: Treatment of the atonic bladder. *Trans. Am. Assoc. Genito-Urin. Surgeons*, 27: 99, 1934.
- BROWN, W. E.: Postoperative urethrocystitis in gynecologic patients: its prophylaxis. *Univ. Hosp. Bull. Ann Arbor*, 3: 78, 1937.
- BUERGER, LEO: Pathological diagnosis of tumors of the bladder with particular reference to papilloma and carcinoma. *Surg. Gynec. Obst.*, 21: 179, 1915.
- BUMPUS, H. C., AND SILVER, B.: Tumors of the bladder. *J. Urol.*, 37: 141, 1937.
- BUTTERFIELD, P. M.: Experiences with a new baby cysto-urethroscope. *Am. J. Surg.*, 8: 102, 1930.
- CABOT, H., AND PACE, J. M.: Method of selecting proper operative treatment in cancer of the bladder. *Trans. Am. Assoc. Genito-Urin. Surg.*, 30: 201, 1937.
- CAHILL, G. F.: Rupture of the bladder and urethra. *Am. J. Surg.*, 36: 653, 1937.
- CAMPBELL, M. F.: Rupture of the bladder: clinical study of 55 cases. *Surg. Gynec. Obst.*, 49: 540, 1929.
- CAMPBELL, M. F.: Trigonal curtain obstruction of the bladder outlet. *J. Urol.*, 27: 157, 1932.
- CARSON, W. J.: Gangrene of the bladder. *Ann. Surg.*, 85: 269, 1927.
- CAULK, JOHN R.: Incrusted cystitis. *Trans. Am. Assoc. Genito-Urin. Surg.*, 9: 23, 1914.
- CAULK, JOHN R.: The upper urinary tract in carcinoma of the bladder. *Ann. Surg.*, 101: 1432, 1935.
- CHAUVIN, E.: Ulcération vésicale par application de radium sur le col utérin. *Bull. Soc. franc. d'urolog.*, p. 237, 1935.
- CHAUVIN, E.: Tumeurs vésicales à structure d'adénome. *J. d'urolog.*, 42: 521, 1936.
- CHEETHAM, JOHN G.: Presacral neurectomy for the relief of certain types of bladder dysfunction and pain. *J. Urol.*, 37: 1, 1937.
- CRISHOLME, A. E., AND TUDHOPE, G. R.: Malakoplakia of the urinary bladder. *Edinburgh M. J.*, N. S. 41: 626, 1934.

- CHRISTOPHERSON, J. B., AND WARD, R. O.: Bilharzia disease in England: cystoscopic appearance of the bladder before and after intravenous injections of sodium antimony tartrate. *Brit. J. Surg.*, 21: 632, 1934.
- COLBY, F. H.: Carcinoma of the colon involving the bladder. *Trans. Am. Assoc. Genito-Urin. Surg.*, 28: 199, 1935.
- COLSTON, J. A. C., AND LEADBETTER, W. F.: Infiltrating carcinoma of the bladder. *J. Urol.*, 36: 669, 1936.
- Committee on Carcinoma Registry, Am. Urol. Assoc.: Cancer of the bladder. a study of 902 epithelial tumors of the bladder. *J. Urol.*, 31: 423, 1934.
- Committee on Carcinoma Registry, Am Urol Assoc.: Tenth Anniversary Report. *J. Urol.*, 39: 456, April 1938.
- CRABTREE, E. G.: Changes in the urinary tract in women, the result of normal pregnancy. *New England J. M.*, 205: 1048, 1931.
- CRABTREE, E. G., AND PRATHER, G. C.: Urinary diseases in pregnancy: a consideration of preventive and therapeutic measures in treatment and conservation surgery. *J. Urol.*, 26: 499, 1931.
- CRABTREE, E. G.: End-results of urinary tract infections associated with pregnancy. *Am. J. Obst. & Gynec.*, 34: 405, 1937.
- CREEVY, C. D.: Treatment of the overflow incontinence of neurogenic vesical dysfunction. *J. Urol.*, 35: 507, 1936.
- CRENSHAW, J. L.: Late results in panmural fibrosis of the bladder. *Trans. Am. Assoc. Genito-Urin. Surgeons*, 27: 109, 1934.
- CULVER, H., AND HOEPPNER, W. F.: Bilharziasis of the bladder. *J. Urol.*, 27: 189, 1932.
- CUMMING, R. E., AND NELSON, R. J.: Actinomycosis of the urinary tract. *Surg. Gynec. Obst.*, 49: 352, 1929.
- DAVIES, J. W.: The cystocele: its anatomical disturbance and reconstruction. *Surg. Gynec. Obst.*, 62: 349, 1936.
- DAVIS, E.: Anilin (triphenylmethane) dyes in the treatment of Hunner's ulcer. *J. Urol.*, 46: 899, 1941.
- DAVIS, E. G.: Urinary antiseptics. *J. Urol.*, 5: 215, 1921.
- DEAN, A. L.: The use of radium and the roentgen rays in the management of cancers of the genito-urinary organs. *New England J. M.*, 206: 1078, 1932.
- DEAN, A. L.: Injury of the urinary bladder following irradiation of the uterus. *J. Urol.*, 29: 559, 1933.
- DEBENHAM, R. K.: Investigation of 742 cases of hematuria. *Brit. J. Surg.*, 21: 44, 1933.
- DEMING, C. L.: Primary bladder tumors in the first decade of life. *Surg. Gynec. Obst.*, 39: 432, 1924.
- DEMING, C. L.: The treatment of pyogenic cystitis. *New England J. M.*, 217: 1069, 1937.
- DETARNOWSKY, G.: Rupture of the bladder: plea for its early diagnosis and treatment. *J. A. M. A.*, 95: 476, 1930.
- DICKSON, W. E. C., *et al.*: Malakoplakia vesical; an investigation of certain mycotic infections of the genito-urinary tract. *Urol. & Cutan. Rev.*, 31: 611, 1927.
- DIXON, C. F., AND STROHL, E. L.: Spontaneous rupture of the bladder. *Am. J. Surg.*, 33: 110, 1936.
- DUROEUX, LOUIS: Syphilis de la vessie. *Thèse de Paris*, 1913.
- EATON, J. H.: Hunner ulcers of the female bladder: review of cases. *Urol. & Cutan. Rev.*, 46: 304, 1942.
- ESCOMEL, E.: Trichomonas de la vessie. *Bull. Soc. path. exat.*, 19: 697, 1926.
- EVANS, E. E.: Causative agents and protective measures in the anilin tumor of the bladder. *J. Urol.*, 38: 212, 1937.
- EWING, JAMES: Neoplastic Diseases. *Phila.*, W. B. Saunders Co., 1928.

- FARMAN, F.: Incontinence of urine in women. *J. Urol.*, 44, 841, 1940.
- FARR, R. E., AND BRUNKOW, C. W.: Hernia of the bladder: a brief review of literature, etc. *Ann. Surg.*, 72: 264, 1925.
- FERGUSON, R. S.: Clinical significance of aniline tumor. *J. Urol.*, 38: 243, 1937.
- FERRIER, P. A.: Vesico-sigmoidal fistula. *Urol. & Cutan. Rev.*, 42: 194, March 1938.
- FILLIS, R. E.: Rupture of the bladder. *J. Urol.*, 29: 601, 1933.
- FINESTONE, E. O.: Syphilis of the bladder. *Surg. Gynec. Obst.*, 62: 93, 1936.
- FISTER, G. M.: Similarity of interstitial cystitis (Hunner's ulcer) to lupus erythematosus. *J. Urol.*, 40: 37, July 1938.
- FOLSON, A. I., AND O'BRIEN, H. A.: Transvesical alcoholic injection for elusive ulcer of the bladder. *J. Urol.*, 37: 808, 1937.
- FRANCHINI, G.: Un nuovo caso di buba brasiliana contemporaneo ad affezione da eotamoeba histolytica, etc. *Arch. ital. di sci. med. colon*, 9: 387, 1928.
- FULLER, EUGENE: Extraperitoneal rupture of the bladder. *J. A. M. A.*, 63: 2114, 1914.
- FULLERTON, A.: Observations on bladder injury in warfare. *Brit. J. Surg.*, 6: 24, 1918.
- GARSHWILER, W. P.: Foreign bodies in the urinary bladder. *Am. J. Surg.*, 22: 199, 1933.
- GAUTIER, E. L.: Gomme syphilitique de la vessie. *Bull. Soc. franc. d'uro.*, 6: 291, 1927.
- GAY, D. M.: Pathology of aniline tumor of the bladder. *J. Urol.*, 38: 221, 1937.
- GERHARD. Quoted by Kass.
- GEYERMAN, P. T.: Medical curiosities (snake in bladder). *J. A. M. A.*, 118, 1409, 1937.
- GOLDEY, A.: Bilharziasis with chyluria: report of case and its cure. *Urol. & Cutan. Rev.*, 41: 89, 1937.
- GOVERNEUR, R., et al.: Fistula vesicocolique, etc. *J. de chir.*, 51: 215, February 1938.
- HAGER, B. H.: Clinical data on alkaline incrustrated cystitis. *J. Urol.*, 16: 447, 1926.
- HAGER, R. B., AND MAGATH, T. B.: The etiology of incrustrated cystitis with alkaline urine. *J. A. M. A.*, 85: 1352, 1925.
- HAGNER, F. R.: The bulgarian bacillus in the treatment of cystitis and pyelitis with alkaline urine. *Surg. Gynec. Obst.*, 21: 95, 1915.
- HANSEMAN, D. VON: Ueber malakoplakie der harnblase. *Virchow's Arch. f. path. Anat.*, 173, 302, 1903.
- HARLOW, F. W., AND ATIFI, M.: Some observations on the diagnosis and treatment of bilharziasis of the urinary tract. *Urol. & Cutan. Rev.*, 34: 575, 1930.
- HARVEY, D. F., AND TENNANT, R.: Primary neurogenic sarcoma of the bladder in an infant one month of age. *Am. J. Path.*, 10: 125, 1934.
- HECKEL, N. J.: A study of the pathologic alterations in the female bladder and urethra resulting from infection with trichomonas vaginalis. *J. Urol.*, 35: 520, 1936.
- HEINECK, S., quoted by Farr, Brunkow and Wakeley.
- HERBST, R. H., BAUMBUCKER, G. O., AND GERMAN, K. L.: Elusive ulcer (Hunner) with experimental study of etiology. *Am. J. Surg.*, 38: 152, 1937.
- HERGER, C. C.: Actinomyces of the bladder. *J. Urol.*, 29: 739, 1933.
- HESLIN, J. E., AND MILNER, W. A.: Primary carcinoma in a bladder diverticulum: Pre-operative diagnosis: 6-year cure. *Urol. & Cutan. Rev.*, 42: 365, May 1938.
- HEUSCH. Quoted by Kass.
- HIGGINS, C. C.: Production and solution of urinary calculi. *J. A. M. A.*, 104: 1299, 1935.
- HIGGINS, C. C.: Benign tumors of the bladder. *Ann. Surg.*, 93: 886, 1931.
- HIGGINS, C. C.: Vesicointestinal fistula. *J. Urol.*, 36: 694, 1936.
- HINMAN, FRANK: The principles and practice of urology. P. 932. Phila., W. B. Saunders Co., 1936.
- HINMAN, FRANK: The etiology of vesical diverticulum. *J. Urol.*, 3: 207, 1919.
- HINMAN, F., AND WESSON, M. B.: The trigone of the bladder as a factor in urinary obstruction, etc. *Surg. Gynec. Obst.*, 41: 1, 1926.

- HUEPER, W.: Cystitis emphysematosa. *Am. J. Path.*, 2: 159, 1926.
- HUEPER, W., *et al.*: Experimental investigation on the etiology of aniline tumors. *J. Indus. Hyg. & Toxicol.*, 20: 85, 1938.
- HUEPER, W.: Aniline Tumors. *Arch. Path.*, 25: 856, 1938.
- HUNNER, G. L.: A rare type of bladder ulcer in women. *South. Surg. & Gynec. Trans.*, 27: 247, 1914.
- HUNNER, G. L.: Unusual obstetric injury, causing detachment of bladder and urethra from symphysis pubis and complete epispadias. *Am. J. Obst. & Gynec.*, 34: 840, 1937.
- HUNT, ROBERT W.: Rhabdomyosarcoma in the lower urinary tract. *N. Y. State J. Med.*, 43: 513, 1943.
- HUPP, F. LE M.: Intraperitoneal rupture of the urinary bladder. *Southern M. J.*, 18: 209, 1925.
- JECK, H. S.: Traumatic rupture of the bladder with unusual features. *Internat. J. Surg.*, 32: 56, 1919.
- JECK, H. S.: Removal of foreign bodies from the urethra and bladder. *Am. J. Surg.*, 36: 197, 1937.
- JOLY, J. S.: The etiology of stone. *J. Urol.*, 32: 541, 1934.
- JOLY, J. S.: Stone and calculus disease of the urinary organs. *St. Louis, C. V. Mosby Co.*, 1929.
- JUDD, E. S., AND SCHOLL, A. J., JR.: Diverticula of the urinary bladder. *Surg. Gynec. Obst.*, 38: 14, 1924.
- KASS, I. H.: Neurofibromatosis of the bladder. *Am. J. Dis. Child.*, 44: 1040, 1932.
- KELLY, H. A., *et al.*: Cystocele. *Gynecology*, Chapt. XIX (G. C. Ward), p. 313. *N. Y., D. Appleton & Co.*, 1928.
- KERR, J. M., *et al.*: Combined text-book of obstetrics and gynecology. Ed. 2. Edinburgh, E. and S. Livingstone, 1933.
- KIDD, FRANK: Cystogram of hernia of the bladder. *Brit. J. Urol.*, 2: 166, 1930.
- KIMLA, R.: Von Hansemann's malakoplakia vesicae urinae und ihre beziehungen zur plaque formigen tuberkulose der harnblase. *Virchow's Arch. f. path. Anat.*, 184: 469, 1906.
- KIRWIN, T. J.: Types of vesical neck obstruction suited to intraurethral resection, advantages of treatment by the rotary prostatic resectoscope. *Am. J. Surg.*, 19: 1, 1933.
- KIRWIN, T. J.: The problem of bladder tumors. *Southern M. J.*, 32: 398, 1939.
- KIRWIN, T. J.: Papillomatosis of the bladder: new conceptions of etiology and treatment. *J. Urol.*, 49, 1, 1943.
- KIRWIN, T. J., AND HAWES, G. A.: The diagnostic value of residual urine estimation. *J. Urol.*, 41: 413, March 1939.
- KOSTER, E. A.: Actinomycosis of the bladder wall. *Deutsch. Ztschr. f. Chir.*, 181: 60, 1923.
- KRETSCHMER, H. L.: Elusive ulcer of the bladder. *Surg. Clinic. Chicago*, 4: 1241, 1920.
- KRETSCHMER, H. L.: Leukoplakia of the bladder and ureter. *Surg. Gynec. Obst.*, 31: 325, 1920.
- KRETSCHMER, H. L.: Hematuria: clinical study based on 933 consecutive cases. *Surg. Gynec. Obst.*, 40: 683, 1925.
- KRETSCHMER, H. L.: Leukoplakia of the urinary organs. *Surg. Gynec. Obst.*, 47: 145, 1928.
- KRETSCHMER, H. L.: Xanthin calculi: report of case and review of the literature. *J. Urol.*, 38: 183, 1937.
- KRETSCHMER, H. L.: Elusive ulcer of the bladder: report of 138 cases. *J. Urol.*, 42: 385, 1939.
- KRETSCHMER, H. L., AND DOERING, P.: Leiomyosarcoma of the urinary bladder. *Arch. Surg.*, 28: 274, February 1939.
- KREUTSMANN, H. A. R.: The treatment of Hunner's ulcer with deep x-ray therapy. *J. Urol.*, 46, 907, 1941.

- LANE, C. R., AND MORSON, A. C.: Tumor at the bladder apex involving the urachus. *Brit. J. Urol.*, 2: 272, 1930.
- LANMAN, T. H., AND MOORE, JOHN H.: The surgical significance of urinary incontinence in infants and children. *New England J. M.*, 219: 777, 1938.
- LAZARUS, J. A.: Tuberculosis of the bladder; postoperative management of cases following operations, with special reference to the influence of deep roentgenotherapy. *Urol. & Cutan. Rev.*, 41: 550, 1937.
- LAZARUS, J. A., AND ROSENTHAL, A. A.: Present status, diagnosis, and treatment of common tumors of the bladder, etc. *Urol. & Cutan. Rev.*, 39: 802, 1935.
- LEADBETTER, W. F., AND COLSTON, J. A. C.: Brain metastasis in carcinoma of the bladder. *J. Urol.*, 38: 267, 1937.
- LELAND, H. L.: Vesicointestinal fistula. *New England J. M.*, 213: 45, 1935.
- LETT, HUGH: Urinary calculus, with special reference to stone in the bladder. *Brit. J. Urol.*, 8: 205, 1936.
- LEVIN, H. A.: Gas cysts of the urinary bladder. *J. Urol.*, 39: 45, January 1938.
- LEVY, W. E., AND TRIPOLI, C. J.: Gummas of the bladder. *Am. J. Obst. & Gynec.*, 25: 743, 1933.
- LOWER, W. E.: Vesicovaginal and rectovaginal fistula, etc. *J. Urol.*, 26: 141, 1931.
- LOWSLEY, O. S., AND KIRWIN, T. J.: A clinical and pathological study of congenital obstruction of the urethra. 4 cases. *J. Urol.*, 31: 497, 1934.
- MACALPINE, J. B.: Hemangioma of the bladder: 2 cases. *Brit. J. Surg.*, 18: 208, 1930.
- MAKAR, N.: Cystoscopic appearance of bilharziasis. *Brit. J. Urol.*, 4: 209, 1932.
- MAKAR, N., AND URQUEHART, A. L.: Adenoma of the urinary bladder. *Brit. J. Urol.*, 2: 384, 1930.
- MCCAQUE, E. J.: Incidence and prevention of vesical calculi in the fracture and traumatic group. *Am. J. Surg.*, 38: 85, 1937.
- MCCARTHY, J. F., STEPITA, C. T., AND HALPERIN, S. J.: Sarcoma of the Bladder. *Am. J. Surg.*, 7: 229, 1929.
- MEADS, A. M.: Hunner ulcer. *Urol. & Cutan. Rev.*, 38: 631, 1934.
- MELTZER, M.: Chronic alkaline encrusted cystitis: cure of case with contraction of bladder by vitamin A regime and indwelling catheter. *N. Y. State J. Med.*, 37: 865, 1937.
- MILLER, N. F.: Birth injuries of the bladder and bowel. *Calif. & West. Med.*, 47: 371, 1937.
- MILLS, R. G.: Cystitis emphysematosa. *J. Urol.*, 23: 289, 1930. Also: *J. A. M. A.*, 94: 321, 1930; *J. Urol.*, 24: 217, 1930; *Surg. Gynec. Obst.*, 51: 545, 1930; *Am. J. Obst. & Gynec.*, 20: 688, 1930.
- MINTZ, E. R.: Sarcoma of the bladder in children: case. *New England J. M.*, 205: 756, 1931.
- MONTAGNE, M.: Thérapie de la bilharziose vésicale à schistosomum haematobium. *Gaz. Med. de France*, p. 569, 1933.
- MOORE, J. G., AND ALTMAN, C. C.: Cancer of the bladder. *Amer. J. Surg.*, 44, 135, 1940.
- MOORE, NEIL S.: Diverticulum of the urinary bladder. *Southern M. J.*, 30: 263, 1937.
- MORRIS, M.: Gumma of the bladder. *Indiana M. J.*, 16: 5, 1897-98.
- MULLER, M., AND MACQUET, P.: Corps étrangers de l'uretère et de la vessie. *Ann. de med. leg.*, 18: 447, June 1938.
- NELIGAN, G. E.: Treatment of cystitis. *Brit. M. J.*, 2: 642, 1936.
- NESBIT, R. M., AND GORDON, W. G.: Surgical treatment of the autonomous neurogenic bladder. *J. A. M. A.*, 117: 1935, 1941.
- NITSCHKE, P. H.: Trichomonas infestation of the bladder. *Western J. Surg.*, 45: 278, 1937.
- O'CROWLEY, C. R.: Carcinoma of the bladder. *Ann Surg.*, 101: 1407, 1935.
- O'NEIL, R. F.: Necrosis of the bladder with exfoliation. *Surg. Gynec. Obst.*, 10: 503, 1910.
- ORMOND, J. K.: Interstitial cystitis. *J. Urol.*, 33: 576, 1935.
- OUGLEV, R.: La gangrène vésicale. *J. d'Urol. Med. et Chir.*, 32: 120, 1931.

- PARMENTER, F. J., AND LEUTENEGGER, C. J.: Bladder tumors. *J. Urol*, 35: 316, 1936.
- PATCH, F. S.: Association between leukoplakia and squamous-cell carcinoma in the upper urinary tract. *New England J. M.*, 200: 423, 1929.
- PEACOCK, A. H.: Diverticula of the urinary bladder. *Northwest Med.*, 34: 355, 1935.
- PEACOCK, A. H.: Rupture of the urinary bladder. *Northwest Med.*, 39: 248, 1940.
- PEACOCK, A. H., AND CORBETT, D. G.: Primary carcinoma in a diverticulum of the urinary bladder. *J. Urol*, 25: 625, 1931.
- PEARSE, R.: Choice of treatment in cancer of the bladder. *Canadian M. A. J.*, 34: 30, 1936.
- PEDERSON, JAMES: Syphilis of the bladder. *Med. Rec.*, 90: 235, 1916.
- PENA, A., AND PENAL, E. DE LA: Continuous irrigation in the treatment of alkaline incrustated cystitis. *Urol. & Cutan. Rev.*, 40: 314, 1936.
- PENFIELD, W., AND YOUNG, A. W.: The nature of von Recklinghausen's disease and the tumors associated with it. *Arch. Neurol. & Psychiat.*, 23: 320, 1930.
- PETERSEN, ANDERS: Syphilis of the bladder. *Calif. State J. M.*, 21: 431, 1923.
- PODSYPANINA, N. B.: Die muskeln des trigonum vesicae. *Ztschr. urol. chir.*, 28: 620, 1934.
- POLSE, M. L.: Extraperitoneal rupture of the bladder in transurethral prostatectomy. *J. Urol.*, 46: 528, 1941.
- POSADAS, J.: Leukoplakia. *Argentina Med.* 1905. Abstracted in *Ann. des mal d'voies Gen. Urin.*, 24: 58, 1906.
- PRICE, P. B.: Bladder stone. *China M. J.*, 48: 462, 1934.
- PUTSCHER, W.: Cystitis emphysematosa. Lubarsch-Henke "Handbuch der Spez. path. Anatomie und Histologie," 6(2): 371 Berlin, Jules Springer, 1934.
- RABSON, S. M.: Leukoplakia and carcinoma of the urinary bladder. case: review of the literature. *J. Urol*, 35: 321, 1936.
- RACIC, J.: Calculus of the bladder in Dalmatia. *Urol. & Cutan. Rev.*, 39: 158, 1935.
- RANDALL, A., AND CAMPBELL, E. W.: Alkaline incrustated cystitis. *J. Urol*, 37: 284, 1937.
- RATHBUN, N. P.: Bladder diverticulum complicated by carcinoma of cloacal origin. *Am. J. Surg.*, 8: 627, 1930.
- RATHBUN, N. P.: Primary bladder tumors in infants and young children. *Surg. Gynec. Obst.*, 64: 914, 1937.
- RAVICH, A., AND KATZEN, P.: Cystitis emphysematosa. Review of literature, with report of authentic case terminating in recovery. *J. A. M. A.*, 96: 1256, 1932.
- REDEWILL, F. H.: Cystitis cystica emphysematosa. *Urol. & Cutan. Rev.*, 38: 537, 1934.
- RIBA, L. W., AND PERRY, E.: Trichomonas prostatico-vesiculitis. *J. Urol.*, 22: 563, 1929.
- RIBA, L. W., AND CHRISTENSEN, F. A.: Bilharziasis. *J. Urol*, 32: 529, 1934.
- ROSE, D. K.: The urinary bladder, myogenic and neurogenic. *J. Urol*, 46: 257, 1941.
- ROSEDALE, R. S.: Cystitis emphysematosa: case. *Am. J. Obst. & Gynec.*, 31: 123, 1936.
- ROSENTHAL, D. B.: Urinary infection with trichomonas vaginalis in the male. *M. J. Australia*, 1: 782, 1931.
- ROUS, PEYTON: The virus tumors and the tumor problem. *Am. J. Cancer*, 28: 236, 1936.
- ROUS, P., AND BEARD, J. W.: A virus-induced mamillian growth, with the character of a tumor (Shope rabbit papilloma). *J. Exp. Med.*, 60: 701, 1934.
- ROUS, P., BEARD, J. W., AND KIDD, J. G.: Observations on the relation of the virus causing rabbit papilloma to the cancers deriving therefrom. II. The evidence provided by the tumor; general considerations. *J. Exp. Med.*, 64: 401, 1936.
- ROYSTON, G. D., AND ROSE, D. K.: A new operation for cyclocele. *Am. J. Obst. & Gynec.*, 33: 421, 1937.
- RUPP, I.: Actinomycosis of the bladder wall. *Deutsche. Ztschr. f. chir.*, 211: 208, 1928.
- SANES, S., AND DOROSCHAW, G. D.: Cystitis emphysematosa: 2 cases. *J. Urol*, 32: 278, 1934.
- SCHAPIRO, S. W.: Gummatous ulcerations of the bladder. *Am. J. Surg.*, 29: 213, 1915.

- SCHOLL, A. J., JR.: Squamous-cell carcinoma of the urinary bladder. *Arch. Surg.*, 3: 336, 1921.
- SCHILLINGS, M.: Les angiomes de la vessie. *Rév. belge sc. méd.*, 3: 412, 1931.
- SHAW, F. W.: Human nectrobacillosis infection by actinomyces (bacillus) necrophorus (B. diphtheriae vitulorum). *Stralbl. t. Bakt. (Abt. 1)* 129: 132, 1933.
- SIDDALL, A. C.: Primary calculus of the bladder. *J. Urol.*, 37: 268, 1937.
- SMITH, GEORGE G.: Ulcers of the bladder following the application of radium to the uterus. *New England J. M.*, 207: 822, 1932.
- SPENCE, HARRY M.: Urologic aspects of enuresis. *Southern M. J.*, 34: 831, 1941.
- STEVENS, A. R.: Leukoplakia of the bladder and diverticulum resembling carcinoma. *Trans. Am. Assoc. Genito-Urin. Surg.*, 21: 249, 1928.
- STEVENS, A. R., AND DELZELL, W. R.: Traumatic injuries of the bladder, with report of 27 patients operated upon. *J. Urol.*, 38: 475, 1937.
- STIRLING, W. C.: Cystitis follicularis, etc. *J. A. M. A.*, 112: 1326, April 8, 1939.
- STIRLING, W. C., AND HOPKINS, G. A.: Gangrene of the bladder: review of 207 cases: report of 2 cases. *J. Urol.*, 31: 517, 1934.
- STRACHSTEIN, A.: Syphilitic and parasymphilitic affections of the urinary bladder. *N. Y. Med. J.*, 1916.
- TENENBAUM, G., AND SAIFER, S.: Necrosis of the bladder. *Am. J. Surg.*, 38: 378, 1937.
- THOMAS, FRANK D.: Entomeha histolytica involving the urinary tract. *Urol. & Cutan. Rev.*, 40: 199, 1936.
- THOMAS, GILBERT J., KINSELLA, T. J., AND VAN WINKLE, C. C.: Treatment of tuberculosis of the urinary bladder. *Trans. Am. Assoc. Genito-Urin. Surg.*, 27: 55, 1934.
- THOMPSON, G. J., AND STEIN, J. J.: Leukoplakia of the urinary bladder; report of 34 clinical cases. *J. Urol.*, 44: 639, 1940.
- THOMSON-WALKER, J. W.: The treatment of the bladder in spinal injuries in war. *Brit. J. Urol.*, 9: 217, 1937.
- TOWNSEND, T. M., AND FRUNKIN, J.: Gangrenous cystitis. *N. Y. State J. M.*, 37: 939, 1937.
- VALENTINE, J. J.: Leukoplakia of the bladder. *J. Urol.*, 10: 289, 1923.
- VALVERDE, B.: À propos d'un cas de leucoplasie vésicale d'origine syphilitique. *Ann. d. mal. vén.*, 26: 257, 1931.
- VANCE, A. M.: Bladder accidents. *Kentucky M. J.*, 7: 573, 1909.
- VAN DUZEN, R. E.: The cystoscopic appearance of various types of cystoceles. *Southern M. J.*, 23: 58, 1930.
- VAN DUZEN, R. E.: Amebiasis of the urinary bladder. *Urol. & Cutan. Rev.*, 39: 317, 1935.
- VASTOLA, A. P.: Strangulated femoral cystocele. *Ann. Surg.*, 97: 724, 1933.
- VAUGHAN, R. T., AND RUDNICK, D. F.: New and early sign of ruptured bladder. *J. A. M. A.*, 83: 9, 1924.
- VAUX, N. W.: *Edgar's practice of obstetrics* Ed 6. Phila., P. Blakiston's Son & Co., 1926.
- VISCHER, J. W.: Vesical infection with trichomonas vaginalis. *J. A. M. A.*, 92: 2098, 1929.
- WAKELEY, C. P. G.: Hernia of the bladder: its etiology and treatment. *Brit. J. Urol.*, 2: 1, 1930.
- WATSON, E. M.: The developmental basis for certain vesical diverticula. *J. A. M. A.*, 75: 1473, 1920.
- WATSON, E. M.: The trigone surgically considered; its pathology, etc. *J. A. M. A.*, 81: 1758, 1923.
- WEIS, A. G., AND MEYER, R.: Myxosarcome de la vessie chez un enfant. *Rev. franc. de pediat.*, 8: 748, 1932.
- WELLS, H. GIDEON: Cystitis emphysematosa. *J. Urol.*, 39: 391, 1938.
- WESSON, M. B.: Is the use of a catheter ever justified in fracture of the spine? *Urol. & Cutan. Rev.*, 38: 572, 1934.

- WHITE, E. W.: A very rare bladder tumor (fibromyoma) in a child. J. Urol., 26: 253, 1931.
- WHITE, E. W.: Study of certain urological complications associated with fractured pelvis. J. Urol., 29: 295, 1933.
- WILE, U. J., AND KINGERY, L. B.: Etiology of common warts. J. A. M. A., 13: 970, 1919.
- WILMOTH, C. L.: Traumatic rupture of the bladder. Urol. & Cutan. Rev., 42: 38, January 1938.
- WINSBURY-WHITE, H. P.: A case of vesico-colonic fistula. Brit. J. Urol., 9: 157, 1937.
- WISHARD, W. N. JR., *et al.*: Evaluation of various methods of treating bladder tumors. J. Urol., 35: 503, 1936.
- WOLFE, H. D.: Routine cystoscopic examination as a control measure in anilin tumor of the bladder. J. Urol., 38: 216, 1937.
- YOUNG, H. H., AND WESSON, M. B.: The anatomy and surgery of the trigone. Arch. Surg., 3: 1, 1921.



CHAPTER XXXII

OPERATIVE AND NON-OPERATIVE TREATMENT OF THE BLADDER

A. OPERATIVE TREATMENT OF THE BLADDER

Anesthesia

Bladder operations in our clinic are usually done under regional or local anesthesia. Local infiltration anesthesia, with novocaine, 1 per cent, may be used if a cystostomy only is to be performed. Spinal or sacral anesthesia, however, is used in the great majority of bladder operations.

For children and highly nervous patients, general inhalation anesthesia is preferable.

The various methods of producing anesthesia are described in the chapter on Anesthesia in Urology.

Preoperative Preparation

The preoperative preparation of the patient is most important. Usually, if the bladder shows signs of infection, vesical irrigations with suitable antiseptic solutions are given for several days before operation and urinary antiseptics administered orally, but in emergencies these preliminaries must sometimes be dispensed with. Fluids should be taken freely up to the time of operation, unless inhalation anesthesia is to be used.

The patient is prepared in the customary manner in regard to catharsis and enemas. A soapsuds enema is given the evening before the operation, and a sedative, such as phenobarbital or nembutal, 0.1 Gm. to insure a restful night. If regional anesthesia is to be used, the patient is permitted a light breakfast and fluids.

One hour before going to the operating-room he is given additional analgesic medication by mouth. Phenobarbital or nembutal, 0.2 Gm., is satisfactory (Preliminary Medication, p. 191).

Preparation of Operative Field

The skin of the abdomen and pubes is shaved and cleansed with tincture of green soap and warm water, followed by alcohol, 70 per cent,

and sprayed with tincture of merthiolate, 1:1,000, tincture of zephiran, 1:1,000, or other preferred antiseptic.

Just before operation, a urethral catheter is introduced into the bladder and the bladder irrigated and moderately distended with acriflavine,

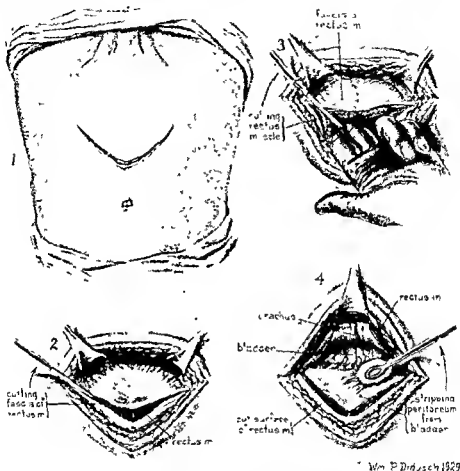


FIG. 239. Suprapubic cystostomy. (1) Inverted-V incision through the skin. (2) The incision is deepened through the fascia of the rectus muscle on each side. (3) The rectus muscle may be cut through, as illustrated here, or separated and retracted. (4) Dissection is carried down along the urachus until the top of the bladder is reached; the peritoneum is then carefully pushed back, exposing the vault of the bladder.

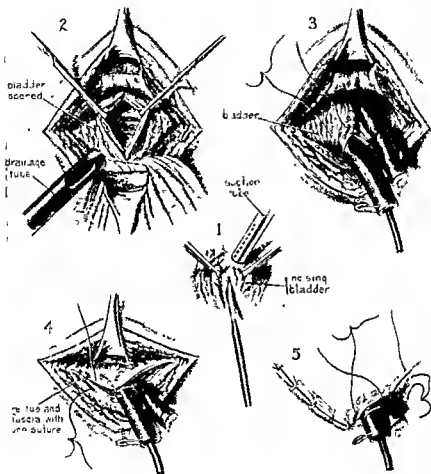
1:6,000, the end of the catheter being clamped to prevent outflow of the fluid.

Position of Patient on Operating-Table

The patient is placed on the operating-table in the Trendelenburg position.

Incisions for Approaching the Bladder

There are a number of incisions for approaching the urinary bladder. The vertical incision in the midline is the one most commonly used.



W. F. D. 1923

FIG. 240. Suprapubic cystostomy. (1) The bladder wall is grasped with Allis clamps,

Some surgeons prefer the transverse incision. The Pfannenstiel curved incision is often considered desirable when wide resection of the bladder, for tumor or diverticulum, is to be done.

Lowsley, in most of his operations upon the bladder, prefers the inverted-V incision. The apex of this should be well above the point to which the dome of the distended bladder would reach. For an ordinary suprapubic cystostomy, the incision is made so that the apex of the inverted-V comes at a point about three-fourths of the distance between the symphysis pubis and the umbilicus. In cases requiring wider exposure of the bladder, such as resection of the bladder for vesical neoplasm with transplantation of a ureter, or resection of a vesical diverticulum, the incision of choice is the Pfannenstiel, which lays open the entire pelvis.

Suprapubic Cystostomy

The incision selected is made through the skin and deepened through the fascia. The recti muscles are either separated or cut across, as indicated. The bladder (distended with acriflavine or rivanol dextrose) is exposed, being recognized by the richness of its blood supply and the characteristic muscle fibers. The wall of the bladder is grasped with Allis clamps. The bladder is then incised to the desired length between the clamps and the irrigating fluid sucked out with the usual protected suction device.

If a plain cystostomy is to be done, a double suction tube (Kenyon) is fixed in place with plain catgut at the highest point in the vesical incision and the highest point in the abdominal wound. The bladder wall is repaired by catgut sutures, one of which is tied around the suction tube. A small cigarette drain is inserted along the suture line of the bladder. The abdominal wound is closed in layers, using plain catgut for the recti and fascia, and, for the skin, interrupted silk, dermal, or silkworm gut sutures, one of which is tied around the double suction tube, fixing its position at the surface. By thus fixing the tube at the highest point in the vesical and skin incisions, the tube is brought through the abdominal wall obliquely.

When the bladder is opened for the purpose of exploring its interior, encroachments on the vesical orifice are noted and the bladder searched for calculi, foreign bodies, tumor, ulceration, diverticulum, etc. Removal of calculi is usually accomplished by the introduction of forceps or a lithotomy scoop. The possibility of more stones being concealed in a diverticulum must always be kept in mind. (The resection of tumor is discussed on page 1106; of diverticulum, on page 1111; of ulcer, on page 1113).

The reader is also referred to the technic of preliminary cystostomy described under Prostatectomy, on page 886.

Resection of the Bladder Wall

Notwithstanding the extensive use of newer methods of treatment—fulguration and diathermy, and irradiation—resection of the bladder wall still has a wide usefulness in a number of vesical conditions, chiefly certain cases of malignant neoplasm, diverticulum, and, less frequently, ulcer and leukoplakia.

RESECTION OF THE BLADDER WALL FOR MALIGNANT TUMOR

Radical resection is the treatment of choice whenever an infiltrating tumor of the bladder is so located that its excision is possible (*Tumors of the Bladder*, p. 1058).

After the diagnosis has been made by biopsy, and the location and extent of the tumor determined by cystoscopy, the surgeon prepares to remove the tumor-bearing portion of the bladder wall with a substantial cuff of healthy tissue. We do not agree with those who free the entire bladder in such cases, believing that wide mobilization disrupts the vesical blood and lymphatic supply to such an extent that necrosis of the entire bladder not infrequently results. In our practice it is therefore customary to mobilize only that part of the bladder to be resected.

Since vesical tumors are often located low down on the lateral wall or trigone, where the growth involves a ureteral orifice, it is frequently necessary to implant the ureter on the involved side to a point higher up on the bladder wall or to the skin of the loin or groin.

Technic. After the site and extent of the tumor have been determined by cystoscopy, the bladder is exposed through a Pfannenstiel, transverse, or inverted-V incision, which is deepened through the fascia, and the recti muscles either separated or cut across, as indicated. The bladder, distended with acriflavine or rivanol dextrose, is grasped with Allis clamps, the wall incised between the clamps, and the contents removed by suction. The tumor is then carefully examined.

The bladder is separated from the surrounding structures just enough to allow of excision of the tumor mass with a wide cuff of normal bladder wall. The vesical wall is incised down to the tumor, and the tumor excised with the scalpel or scissors—rubber-covered Kocher clamps being used to prevent bleeding and necrosis. Great care must be exercised not to squeeze out cancer cells by rough handling of the tumor mass. The surrounding surface is treated with carbolic acid, 50 per cent in glycerine, followed by alcohol, 70 per cent, in order to kill any tumor cells that might have been transplanted.

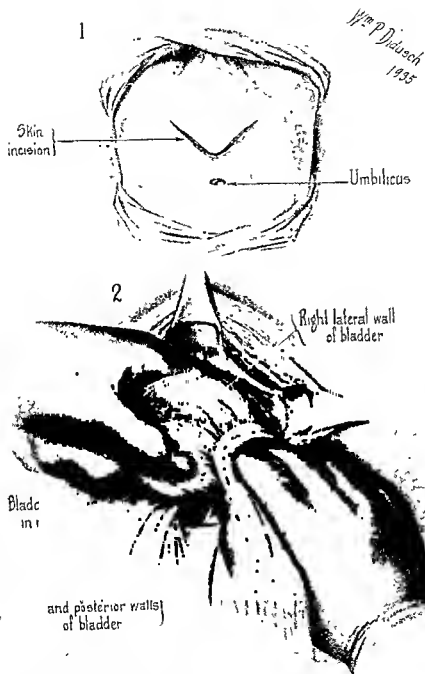


FIG. 241. Resection of bladder tumor. Clamp method. (1) Inverted-V incision. (2) The right lateral and posterior walls of the bladder are freed, after it has been opened in the midline.

A running stitch of plain catgut is used to repair the bladder wall. A double suction tube (Kenyon) is fixed in the highest point of the

bladder wound and the highest point of the skin incision, as this aids in healing. All parts of the exposed area are drained with Penrose drains.

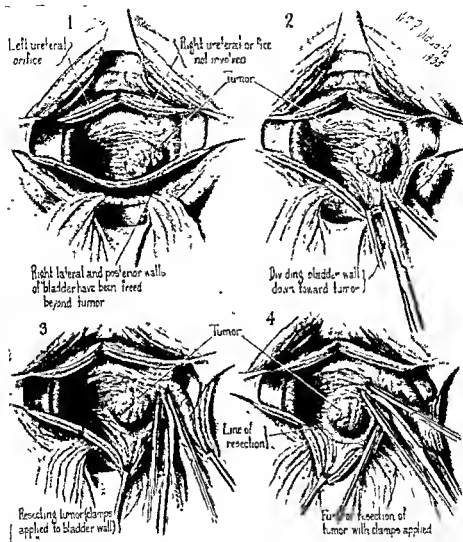


FIG. 242. Resection of bladder tumor. Clamp method. (1) The bladder opened, and the tumor exposed in its position upon the posterior portion of the right wall. (2) The bladder wall is divided down toward the tumor with the cutting instrument. (3) The dotted line shows the cuff of healthy tissue to be removed with the tumor. Clamps are applied to the wall and resection begun. (4) Further resection of tumor, with clamp applied.

The wound is closed in layers, using catgut for the underlying tissues and silk, dermal, or silkworm gut for the skin.

The value of this procedure is enhanced by irradiation after resection

is completed, as we thus take care of any possible extension of the malignant process which may have remained outside the line of resection.

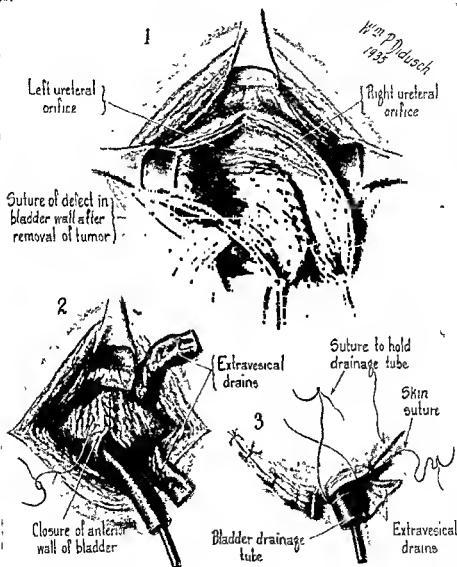
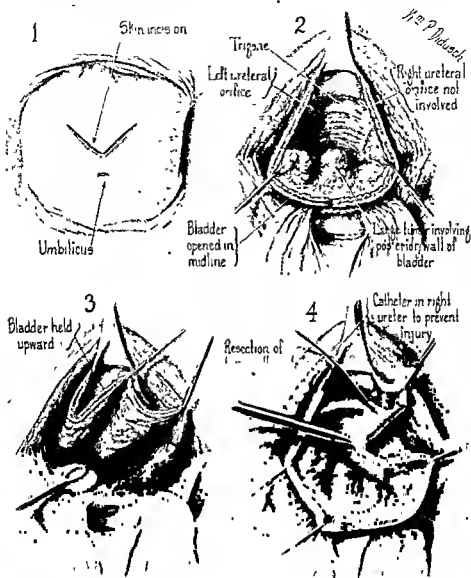


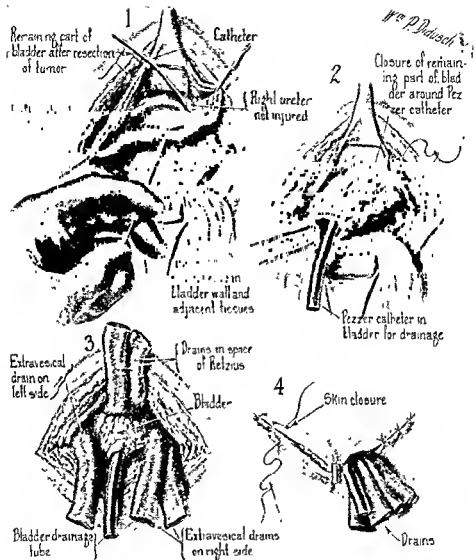
FIG. 317. Operation of bladder tumor. Closure method. (1) The tumor has been resected. (2) The drainage drains are placed in the bladder.

Because a wound in the bladder wall, produced by the cautery or electric wire, causes extensive necrosis which is slow to heal, we think it

wiser to excise the tumor with a scalpel, cauterizing the surface with carbolic acid followed by alcohol. Some surgeons, however, prefer to



excise the tumor with the electrocautery. Radon seeds may be inserted into the cut edges of the wound before closing it.



RESECTION OF VESICAL DIVERTICULUM

Large, retentive diverticula should be surgically removed. A one, two, or three-stage procedure may be done, according to the indications of the particular case. In the three-stage operation described by Lowsley and Gutierrez in 1928, the first stage is drainage of the bladder, to secure

proper excretory function; the second stage, the relief of obstruction due to an enlarged prostate, a congenital valve, or other cause; and the third stage, resection of the diverticulum.

Technic. The bladder, distended with a mild antiseptic fluid, is exposed by the method indicated in the particular case (Incisions for Approaching the Bladder, p. 1104). The wall of the bladder is grasped

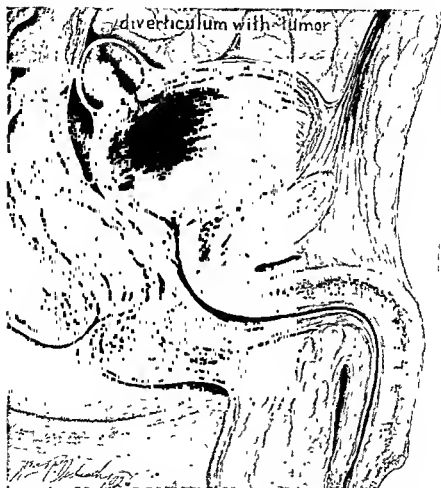
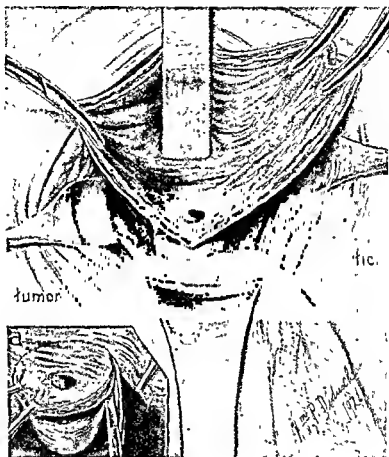


FIG. 246. Large papilloma in a diverticulum of the bladder.

with Allis clamps, punctured, and the viscus drained by suction. The bladder is then opened widely by a long incision between the clamps.

The orifice of the diverticulum is identified and an incision made down the bladder wall to it. The operator's finger is inserted into the diverticulum, and its outer wall is carefully freed from the surrounding structures. After it has been completely isolated, the diverticulum, with its entire orifice, is resected.

The resulting hiatus of the bladder wall is closed with a running catgut suture. All parts of the pelvis that have been exposed are carefully drained with Penrose drains. The bladder wound is closed with catgut, a double suction tube (Kenyon) being fixed in the highest point of the



bladder wound and of the skin incision. The wound is closed in layers, using catgut for the fascia, and silk, dermal, or silkworm gut for the skin.

RESECTION OF THE BLADDER WALL FOR ULCER

Radical resection of the bladder wall for localized submucous fibrosis (Hunner's ulcer) is sometimes indicated (Localized Submucous Fibrosis, p. 1018).

Technic. Resection for ulcer should be kept an extraperitoneal opera-

tion if possible. This can be accomplished in those cases where the disease is limited to the vertex and anterior wall, and it is occasionally possible to separate the involved peritoneum when a portion of the bladder covered by this structure is involved in the ulcerative process. More often, however, it will be impossible to avoid breaking through either the peritoneal covering or the bladder itself. Experience has taught that the best method of separating the peritoneum is first to brush back the vertex portion as far as it will go with ease; then, instead of persisting in trying to carry this separation further down the posterior wall from

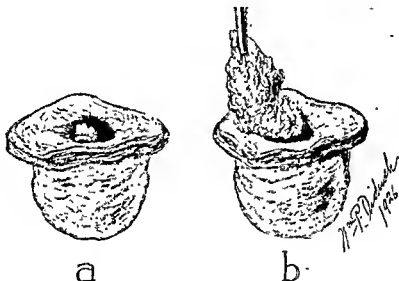


FIG 248. Diverticulum of the bladder containing a tumor (specimen removed at operation) (a) Shows tumor within the diverticulum (b) Tumor drawn outward through the orifice

the vertex, free the lateral walls down to the ureteral region on each side. From near the base, in the lateral or ureteral regions, it will be possible to work toward the midline about the base of the bladder, and, after separating the peritoneum in the ureterovesical region, to come forward on the posterior wall until the entire peritoneum, except the urachal portion, is freed. The freeing of the urachal portion can be done with less danger of entering the peritoneum if done as the final, rather than the first, step of the separation.

The cystoscope should always be used in determining where the bladder should be opened, so that cutting down upon the inflammatory area

may be avoided. For example, if the involved area is to the right of the midline, the incision should be on the midline or a little to the left of it. The vessels should be clamped and tied as they are reached. On opening

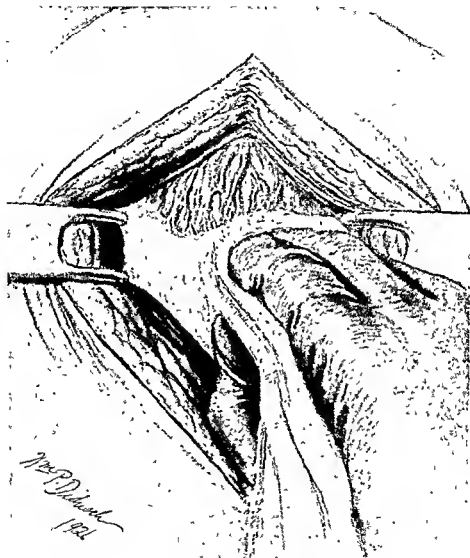


FIG. 249. Diverticulectomy Incision has been made through the skin, and the peritoneum is being stripped from the bladder.

the bladder, the edema, which has arisen since the preliminary cystoscopy, may have caused so much swelling of the mucosa as completely to hide the two or three small ulcers that had been visible through the cystoscope; but in many cases this preliminary examination will cause

so much bleeding from the ulcers that their whereabouts will be easily ascertained.

After the diseased area has been excised, the bladder wall is repaired with a running stitch of plain catgut. A retention catheter should be inserted and sutured to the bladder wall, and all parts of the exposed area drained with Penrose drains. The external wound is closed about the drains in the usual manner.

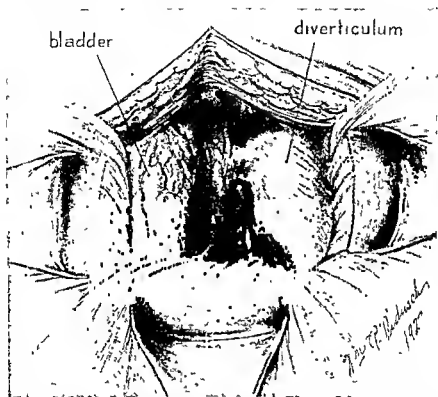
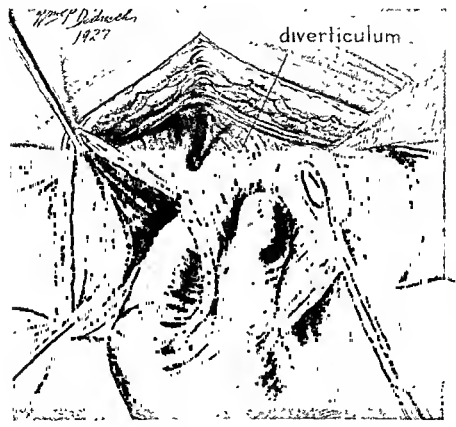


FIG. 250. Diverticulectomy. The diverticulum has been exposed, and its connection with the bladder can be seen.

Postoperative Care. The drains are removed at the end of the second day, and irrigations given through the catheter, employing for this purpose acriflavine or rivanol dextrose, 1:8,000. With the patient on his side, several irrigations should be given at each session, a small amount of fluid being run in and immediately withdrawn. On the tenth to fourteenth day, according to the rapidity with which recovery has taken place, the catheter should be removed, and the irrigations thereafter given through the urethra each day until it can be demonstrated that the bladder is entirely free from infection.

RESECTION OF THE BLADDER WALL FOR LEUKOPLAKIA

Leukoplakia (p. 1019) is preferably treated by resection, if the involved portion of the bladder wall is not too extensive and is so located as to be accessible to surgery. Resection in such cases follows along the same lines as for tumor.

*Cystectomy*

There has been a renewal of interest in recent years in the possibility of curing certain types of carcinoma of the bladder by total cystectomy (Tumors of the Bladder, p. 1059). This has been due primarily to the perfecting of methods of transplanting the ureters. Cystectomy, with ureteral transplantation, is also applicable in the treatment of (1) exstrophy of the bladder, (2) certain cases of vesicovaginal fistula which have

not been benefited by plastic operation, (3) occasionally in very severe and stubborn cases of localized submucous cystitis.

The ureters may be implanted into the skin of the back or groin, or they may be transplanted to the large intestine. The latter is the more ideal procedure, but is not always feasible. When ureterocutaneous anastomosis is done, both ureters are transplanted simultaneously and the bladder subsequently removed together with the seminal vesicles,

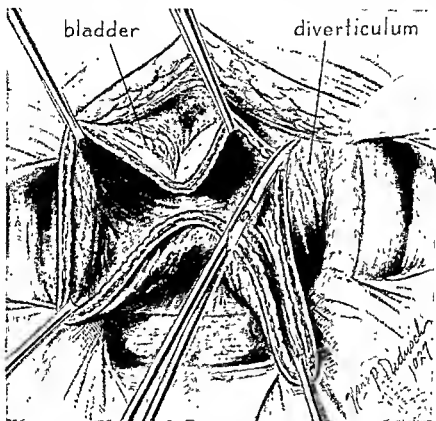


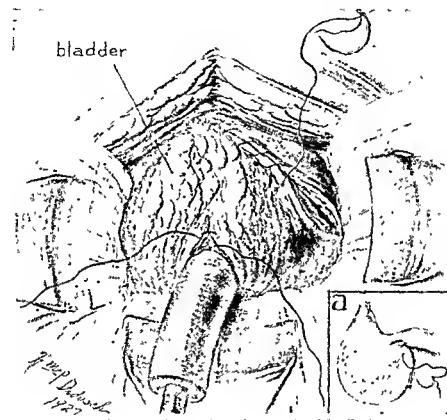
FIG. 252. Diverticulectomy. After it has been completely isolated, the diverticulum, with its entire orifice, is resected. Showing the orifice of the diverticulum opened and the freed portion of the sac being excised.

but leaving the prostate unless its removal is specifically indicated. When the ureters are transplanted to the sigmoid or rectum, the operation is done in three stages, the ureters being transplanted in two operations and the bladder removed after a suitable period has elapsed.

Before subjecting the patient to this serious procedure, he must be put in the best possible physical condition. The length and nature of the preoperative preparation depends upon the state of the renal function

and, if transplantation to the intestine is to be done, upon the condition of the colon. Adequate preoperative preparation will lessen the dangers of postoperative complications.

Transplantation of the ureters is discussed under Operative Treatment of the Ureters (p. 1324).



Technic of Cystectomy. A Pfannenstiel incision is deepened through the subcutaneous tissue and fascia, and the recti muscles either separated or partially severed, in order to expose the pelvic region as fully as possible. The bladder is identified, grasped with Allis clamps, and the fluid with which it is distended is allowed to flow out.

The bladder is carefully dissected free from its surrounding tissues, the blood vessels being severed and ligated as necessary. The seminal vesicles are usually removed with the bladder, the ampulla of the vas on

each side being ligated and cauterized. At the vesical orifice the incision is made to include the entire internal sphincter, but not the prostatic urethra. This is cut across and the severed urethra stitched up.

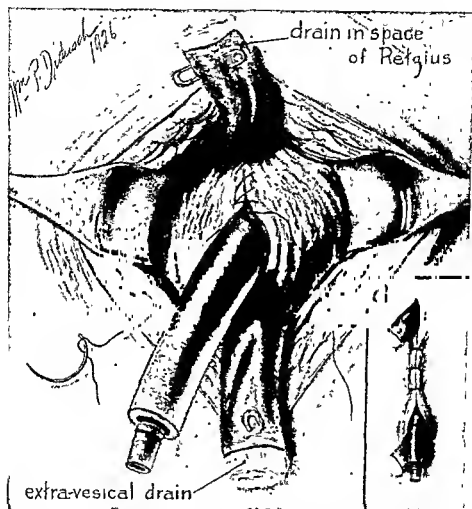


FIG. 254. Diverticulectomy. Method of placing the drainage tube and Penrose drains after the removal of a diverticulum. (a) Closure of the skin.

Many Penrose drains are inserted at the proper places, to carry off the excess serous discharges. The wound is closed in layers, using catgut for the muscles and fascia, and dermal, silk, or silkworm gut for the skin.

Surgical Treatment of Rupture and Wounds of the Bladder

Rupture of the bladder is an emergency condition of the first magnitude. The diagnosis should be made, and surgical treatment instituted,

within a few hours (Injuries to the Bladder, p. 986). Negley (1927) showed that the mortality in operations performed in the first 12 hours was only 11 per cent; in the second 12 hours, 22 per cent; and on the second day, 43 per cent. When the history and findings indicate rupture or a penetrating wound of the bladder, even if the diagnosis has not been definitely established, suprapubic exploration of the bladder is advisable, since delay in treatment is fatal (Suprapubic Cystostomy, p. 1105).

The procedure to be followed will vary with the location of the rupture, the presence or absence of infection, and the associated injuries. In general, the primary aims of surgery are the repair of the rent, drainage of the infiltrated areas, and drainage of the bladder.

The establishing of free suprapubic drainage, at the earliest moment, is of the utmost importance in all cases of bladder rupture, whether the rupture be extraperitoneal or intraperitoneal. In small, uncomplicated extraperitoneal ruptures and wounds, adequate suprapubic bladder drainage may be all that is necessary, if extravasation has not yet set in. In most instances, however, extravasation has already taken place, and abdominal, prevesical, and even perineal drainage may be needed in addition to the cystostomy.

Technic. Intraperitoneal Rupture. If intraperitoneal rupture is present, the fluid is aspirated. The vesical tear is located and repaired with catgut and the peritoneum closed, if the case is seen early, before infection has set in. Suprapubic drainage of the bladder, with a double suction tube, keeps the viscus dry and prevents urinary leakage, and should be maintained until healing takes place. If there has been extravasation of urine into the peritoneal cavity, a drain is placed in the cavity. Flushing out the abdominal cavity in cases of intraperitoneal rupture is considered unnecessary by most authors.

In very extensive lacerations of the bladder and adjacent tissues the precarious condition of the patient may make complete repair inadvisable. In such cases it is wiser to control hemorrhage, provide free drainage, and administer supportive treatment.

Extraperitoneal Rupture. In extraperitoneal rupture the rent usually occurs just behind the interureteral ridge, where it is easily identified and closed with two or three plain catgut sutures. The bladder is then closed around a double suction tube, and the skin incision closed in the usual manner.

Injuries involving the floor of the bladder, and with extravasation into the deep pelvis, may require perineal as well as suprapubic drainage.

Of late years another type of extraperitoneal rupture has occasionally

occurred, namely, rupture at the vesical neck, caused by the electrical loop in vesical neck resection. When this occurs, in spite of the fact that the patient is under spinal anesthesia he will complain bitterly of pain as the fluid passes out into the perivesical tissues. The course of procedure in such instances is *immediate* suprapubic cystostomy, with drainage both inside and outside the bladder, the tear being stitched up if it can be located—which it usually can.

Surgical Treatment of Exstrophy of the Bladder

The treatment of exstrophy of the bladder is entirely surgical. The condition of the victims of this anomaly is so pitiful that any measures for their relief, no matter how uncertain the results, will usually be welcomed by the patient and his relatives. Surgical intervention should be undertaken as early in life as possible, although the deformity has been successfully corrected as late as the fortieth year. Without operation, however, a large proportion of these sufferers die in infancy or early childhood from ascending infection, and few survive the twentieth year (Exstrophy of the Bladder, p. 960).

Three types of operations are used in the effort to correct this condition: (1) plastic operations designed to repair the defect in the bladder wall; (2) transplantation of the ureters to the skin, so that the urine can be collected in a special receptacle; (3) transplantation of the ureters into the rectum or sigmoid and extirpation of the bladder. The last procedure is regarded as best by most surgeons who have concerned themselves with this difficult problem.

Plastic Operations for Repair of the Bladder Defect. The first attempt to reconstruct the bladder in accordance with modern surgical methods was made by Roux in 1852. The most widely employed of the earlier procedures was that of Sonnenberg, performed upon the male. This consisted of freeing the posterior vesical parietes from the peritoneum, covering the exposed peritoneum by two lateral flaps, freeing the ureters beneath the edges of the flaps at the point where the epispadiac urethral sulcus begins, and inserting the ureters into the newly formed bladder wall. These earlier flap operations were attended by a high mortality, and resulted, for the most part, in partial or complete failures.

Of more recent procedures, the most commonly employed have been those of Thiersch and Wood. Wood's operation consists in turning down a piriform flap of skin and fascia from the abdominal wall near the

umbilical region, so that the cutaneous side of the flap will serve as a lining membrane for the new anterior wall of the bladder. Lateral flaps are turned up from the inguinal region and rotated inward toward the median line so that the upper and inner margins are brought into juxtaposition and can be united by interrupted sutures. The surfaces which are left exposed by the turning down of the flaps are either sutured or allowed to heal by granulation. This method requires numerous operations and is, therefore, a decidedly tedious matter. Unless the skin is depilated before the flap is turned down, the hair follicles upon the skin surface (which is now within the bladder) continue to produce hair, which serves to form phosphatic deposits in the artificial vesical cavity and may prove very troublesome. Although the operation reduces the wide expanse from which urine can escape, it in no way relieves the incontinence, and merely makes practicable the use of a receptacle for collecting the urine as it escapes.

Direct union of the fissured edges is sometimes attempted, utilizing the technic of Trendelenburg. He endeavored to do away with the pubic diastasis by cutting through on both sides of the sacroiliac synchondrosis, applying a mechanical device which pressed the symphysis together, and immobilizing the patient for several weeks, the bones being later sutured together. In order to make a sphincter capable of contracting, free incisions were made in the upper wall of the funnel formed by the bladder and in the prostatic urethra, the resulting wound being united by Lembert sutures. According to Thiersch, this technic is only applicable when a large portion of the bladder wall is present; otherwise there would be insufficient material for the formation of a reservoir.

The end-results of these and other plastic procedures have usually been unsatisfactory.

Transplantation of the Ureters to the Skin. The ureters are sometimes brought out through the back (lumbar ureterostomy) or groin (iliac ureterostomy) and transplanted to the skin, so that the urine can be collected in an especially constructed urinal. While the patient in some instances has been able to enjoy a fairly comfortable existence, the urine-collecting apparatus is inconvenient, and ascending infection is common in spite of careful protection of the ureteral openings.

Transplantation of the Ureters to the Large Intestine and Removal of the Bladder. Transplantation of the ureters to the sigmoid or rectum is now generally regarded as the best means of dealing with this distressing condition. It is usually accomplished in two stages. When the

patient has recovered from the operations for deflecting the urine into the bowel, the exstrophied bladder is removed and the defect in the muscular wall repaired by bringing the recti together.

The great drawback to uretero-intestinal transplantation has been the danger of ascending infection, which has persistently nullified the efforts of surgeons through many years. With increase in surgical skill and improvement in aseptic methods, however, this danger has been materially lessened, and the consensus of opinion now is that the danger of infection from a ureter transplanted into the rectum or sigmoid is no greater than that from one exposed in the exstrophied bladder, or from one transplanted to the skin of the back or groin, where it meets with no such natural defense as within the rectum. In addition, transplantation of the ureters to the intestine affords the patient the enormous benefits of sphincteric control, enabling him to live a normal life. Ureteral transplantation is discussed under Operative Treatment of the Ureters (p. 1324).

Operative Treatment of Vesical Calculus and Foreign Bodies

Operation for the removal of vesical calculus is probably the oldest surgical procedure of which we have record. The consideration of methods for removing stones from the bladder looms large in very early medical literature, and the history of surgery during the Middle Ages is almost entirely a record of these attempts. The older procedures were carried out through the perineum (low lithotomy), but with the introduction of better surgical methods and modern conceptions of asepsis, the suprapubic route became the one regularly employed for open operation.

More than a century ago the advantages of crushing the stone by instruments introduced through the urethra were plainly recognized. In 1824 Civiale introduced the first lithotrite, and in 1878 Bigelow, of Boston, employed the modern operation of litholapaxy, in which the calculus is crushed and the fragments evacuated through a metal tube at the same sitting. Since Bigelow's epochal contribution, there has been little change in litholapaxy except the introduction of the visualizing lithotrite.

Choice of Operation. Stones associated with hypertrophy of the prostate, vesical diverticulum, or other conditions for which operation must be done, are usually removed in the course of the prostatectomy or diverticulectomy. Small or medium-sized stones may be removed

through the urethra with a rongeur, such as the Lowsley cystoscopic rongeur (p. 105). Other stones must be removed either through a suprapubic cystostomy incision (suprapubic lithotomy) or by litholapaxy.

The choice of operation depends upon the size and hardness of the stone, the age and physical condition of the patient, the presence or absence of associated urethral, vesical, or vesical neck abnormalities, and the experience of the surgeon.

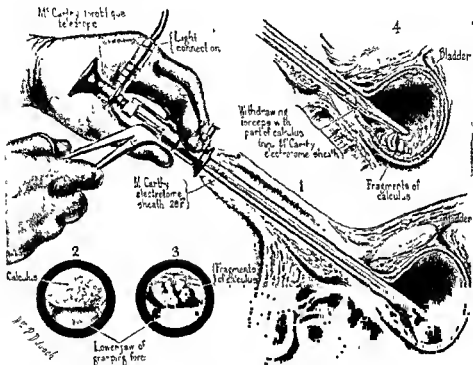


FIG. 205. The suprapubic bladder stone with the Lowsley cystoscopic rongeur. (1) Scissors.

Suprapubic lithotomy is the operation of choice when the stone is large (2 cm. or more in diameter); when there are complications, such as vesical tumor or ulceration (producing bleeding), diverticulum, urethral stricture, marked cystitis, or prostatic obstruction; and when there is advanced renal disease, or the systemic state of the patient is otherwise poor. It is also preferable for the occasional operator, who has not made a special study of the proper technic of litholapaxy.

Only small or medium-sized stones should be crushed by means of a

lithotrite. Large stones are unsuited to crushing. For smaller stones, a visualizing instrument, such as the Kirwin cystoscopic lithotrite (p. 106), is very satisfactory. Litholapaxy is definitely an expert's operation, but in the hands of a skilled operator the mortality is low. Continental surgeons and, particularly, British surgeons who have perfected their technic by extensive experience in the Orient, where vesical stone is common, report a very low mortality. Many of the deaths which have occurred following litholapaxy have been due to rupture of the bladder wall, an accident very unlikely to occur with one who has mastered the proper technic. Bladder rupture appears to be as frequent with the visualizing as with the non-visualizing lithotrites. The mortality in suprapubic lithotomy is usually given as 8 to 10 per cent. These figures, while high for a large clinic with modern facilities, can probably be accepted as a fair average for surgeons in the United States as a whole. (In our own service, the mortality in 73 cases was 4.1 per cent).

Given an experienced operator, the lower mortality of litholapaxy is an advantage, as is also the shorter convalescence; and the procedure should probably be utilized more often than it now is in properly selected cases. A disadvantage of litholapaxy is that recurrences are more frequent by reason of the fragments left behind.

The treatment of foreign bodies in the bladder is, in general, the same as that of calculus. If cystoscopic inspection shows the encrusted mass to be small enough to pass readily through the urethra, it can generally be removed, entire, with the Lowsley cystoscopic rongeur or a similar instrument. Fairly large masses may sometimes be crushed with the lithotrite and removed in fragments; but if the stone is very large, or formed about a very hard object, suprapubic cystostomy is the only recourse.

Suprapubic cystostomy is described on page 1105.

Litholapaxy

Instruments. There are many instruments for crushing and removing stones from the bladder now on the market. These are of two types—visualizing and non-visualizing lithotrites. The latter do not differ fundamentally from the pioneer invention of Bigelow, although numerous modifications of both the lithotrite and evacuator have appeared.

The cystoscopic lithotrite is not as strong as the non-visualizing instrument, and may break if an especially hard stone is encountered and extreme force is applied. For the removal of small stones, however,

it is excellent. Twinem (1936) conducted some very interesting experiments to determine how great this danger of breakage really is. By these tests he was able to ascertain (1) the exact amount of force required to crush calculi of various sizes and compositions; (2) the extreme limits of crushing strength of five lithotrites—four visualizing and one non-visualizing; (3) the ratio of the amount of force required to crush a calculus to the diameter of that calculus. Uric acid stones were found to be the most resistant, with calcium oxalate second, and phosphatic calculi the least resistant. It was found that to crush a uric acid stone, applying force through its smallest diameter of 1.6 cm., a pressure of 162 pounds was required. Therefore, to crush a stone of this composition even 1 inch in diameter (which almost all operators would consider small enough for crushing), would require 200 or more pounds of pressure—an amount greater than the limits of safety of some lithotrites. The blind instrument stood up much better in this test than the cystoscopic lithotrites.

Contraindications to Litholapaxy. Contraindications to litholapaxy are:

- (1) Stones of large size, or of very hard consistency and above a certain size. The hardness of a stone can usually be estimated preoperatively by the kind of x-ray shadow it casts, a study of the urinary crystals, and its cystoscopic appearance.
- (2) Stones in a diverticulum.
- (3) Hypertrophy of the prostate or other vesical neck obstruction, interfering with free movement of the instrument; urethral stricture; or disease of the bladder, such as tumor, ulceration, or severe cystitis.
- (4) Advanced renal disease.
- (5) Poor general health, contraindicating a lengthy procedure. (Litholapaxy takes an hour or more, whereas a suprapubic intervention usually occupies less than half that period.)
- (6) A calculus attached to the bladder wall. (Adherent stones are usually formed upon a suture or a spicule of bone.)
- (7) A stone formed around a solid foreign body which is of such shape and nature as to prevent its removal through the urethra.
- (8) Markedly contracted bladders, making it impossible to introduce enough fluid into the bladder to distend it sufficiently for the proper carrying out of litholapaxy.

Caulk has emphasized the possibility of the operator being misled as

to the amount of contracture of both the urethra and bladder because of muscle spasm. If caudal or spinal anesthesia is used (as is the custom at the Brady Foundation), the resulting relaxation will enable the true capacity readily to be gauged.

Technic of Litholapaxy. The patient is prepared as for other trans-urethral operations. Caudal or spinal anesthesia is preferred by us for this procedure.

The instrument of choice, well lubricated, is introduced through the meatus, and held in the vertical position as it is pushed gently but steadily forward until the beak has attained the lowest portion of the urethral bulb. Care must be taken not to depress the handle of the instrument before reaching the bulb, as this is likely to cause it to catch at a point just external to the opening through the triangular ligament. The turn when the bulb is reached also must be made carefully, else the beak of the instrument may be stopped below the triangular ligament. Lifting the heel of the instrument by placing the fingers of the left hand against the perineum will help the beak to pass easily through the opening, as the fingers can feel it "jump" when the depression before the triangular ligament is reached, and this can be taken as a signal to depress the handle rapidly, whereupon the beak will slide easily into the bladder cavity (Cabot). When the bladder once has been entered, attempts to grasp the stone must take into consideration the danger of seizing a fold of the vesical mucosa; therefore, after locking the jaws of the lithotrite upon the stone, the instrument should be rotated freely before any attempt at crushing the stone is made. If it cannot be rotated, there is a strong likelihood of the mucosa being included in the "bite." Several attempts may be required to crush the stone completely, and, when this is accomplished, great care must be exercised to see that all the fragments are evacuated.

The suction apparatus used for evacuation of the fragments is described on page 1150.

After-care Following Removal of Calculus. This is described under Renal Calculus (Follow-Up Treatment: The Problem of Recurrence, p. 1609).

Repair of Vesicovaginal Fistula

All operations upon vesicovaginal fistulas have for their common objective the restoration of the bladder to its normal function as a reservoir of urine. If the bladder wall can be tightly closed, the vagina will

frequently take care of itself, healing by granulation after a mere freshening of its edges. The bladder floor must be separated from its adherence to the vagina, even if the whole of the detrusor muscle is split sagittally, as recommended by Quinby.

Robert T. Frank observes that often a large fistula resulting from difficult labor, in a bruised and infected birth canal, will heal spontaneously, while a smaller one, apparently far less infected, will require repeated operations and then may fail to heal. He notes that when the bladder is freed and mobilized (either spontaneously during the progress of labor, or purposely at operation), healing often takes place without surgical intervention. Apparently the combination of two factors favors healing: (1) mobilization allows the bladder to contract and thus diminishes the size of the opening; (2) mobilization also favors the gliding and displacement of the tissue planes one upon another, so that broad raw areas come into direct apposition. These two factors probably play a far more important role than points concerning which surgeons evince the greatest anxiety, such as the method of suture or the type of material employed in suturing.

Methods now in use. The methods of repair in usage today are of three types: (1) denudation and suture according to the method of Sims (with modifications); (2) flap-splitting, with separate suture of the bladder wall and vesical mucosa; (3) suprapubic transperitoneal laparotomy.

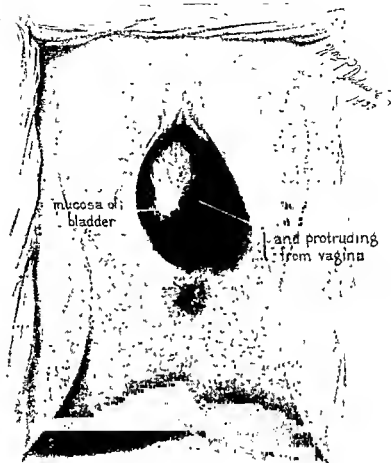
All successful operators recommend the severing of scars which fix the bladder to the pelvic bones.

The usual route of closure is through the vagina. High and inaccessible openings may be attacked suprapubically, usually by the transperitoneal route, though occasionally the transvesical method is advisable. Combined vaginal and abdominal operations may be necessary for patients having extensive scarring.

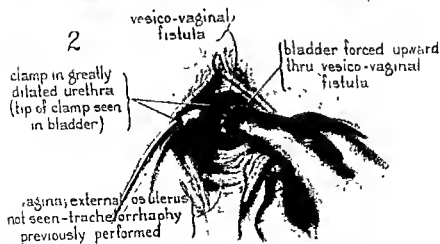
Figures 256 to 260 illustrate a very severe grade of vesicovaginal fistula seen on our service, and the method of repair.

Sims' Operation. Sims' method is too well known to require detailed description here. Its chief features are the use of (1) Sims' position; (2) the "duck-bill" speculum—the forerunner of the Sims' speculum; (3) silver wire and lead clamps for suturing, this being the first occasion of the regular employment of such materials; (4) a self-retaining catheter in the bladder, to keep it free of urine during the entire period of healing. It is this method of Sims, with certain modern refinements, that is still

1



2



regularly employed in most gynecological clinics for lower and more accessible fistulas.

Transvesical Closure. This method, originally proposed by Trendelenburg, was subsequently modified and re-introduced by Hugh H. Young.

The Schuchardt incision is employed for suprapubic exposure of the bladder.

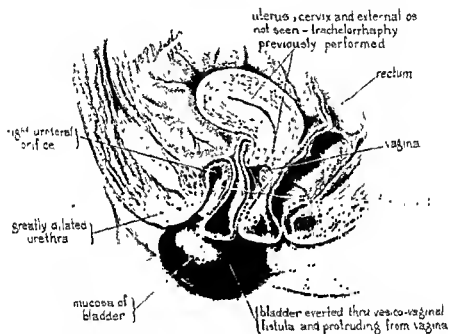
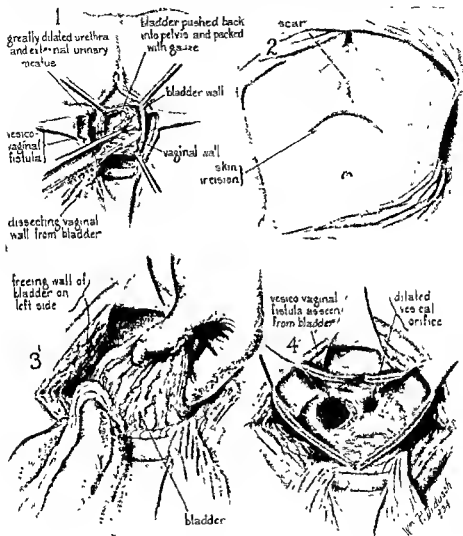


FIG. 257. Repair of vesicovaginal fistula. Sagittal section showing condition present. The bladder, completely everted through the fistulous opening, protrudes through the vulva. The urethra is much dilated. (Kirwin's case.)

The opening of the fistula is elevated by the assistant placing his fingertip in the vagina; or a small hook may be used (Douglass found one made from a safety-pin perfectly satisfactory). Where the cervix has been cut away, this method affords a view of even a very inaccessible fistula.

The mucosa is incised and reflected from the edges, and when these have been sufficiently freshened, the fistula is invaginated into the vagina by the setting and tying of *concentric purse-string* sutures. The mucosa is closed with interrupted chromic catgut stitches (No. 00), the anterior bladder wall with interrupted plain catgut, and the fascia with inter-

ruptured chromic catgut sutures. A suprapubic catheter is left in position, so that the bladder will be continuously free of urine.

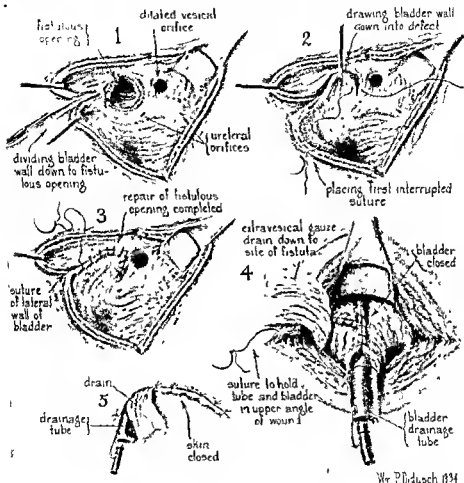


to the left. (Kirwin's case)

The patient is kept lying, face down, upon her abdomen until the repair has healed. This usually requires about 2 weeks, but, in comparison

with years of incontinence, this inconvenience seems trifling to most of these unfortunate women.

Transperitoneal Repair, Using Omental Flap. Waltman Walters has recently reported successful transperitoneal repair of recurring vesico-



vaginal fistula in two cases by closing each fistulous opening separately and then suturing an omental flap between the bladder and the vagina.

Uretero-Intestinal Transplantation. In an occasional case there may be such extensive destruction of tissue that repair is impossible. Such

patients may require transplantation of the ureters to the sigmoid or rectum (*Operative Treatment of the Ureters*, p. 1324).

Time of Operation. Spontaneous healing of fistulas following obstetrical injuries occurs frequently enough to make it wise to wait at least 3 months postpartum before intervening surgically. This period of waiting is not wasted, as it permits complete involution of the genital tract and gives the adjacent tissues time to heal if they have shared in the trauma, which they usually have.

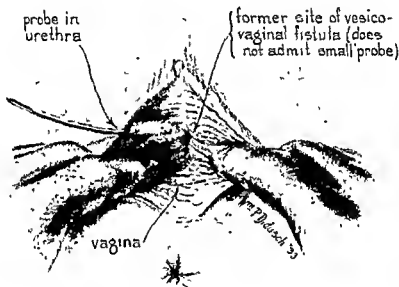


Fig. 460. Location of vesico-vaginal fistula. Result after operation. (W. P. D. 33)

Repair of clean-cut postoperative fistulas may be attempted earlier than that of those resulting from sloughing. In infected cases, 3 or 4 months must usually elapse before the exudate will have absorbed sufficiently to offer a fair chance for operative success.

Sympathetic Surgery for the Relief of Bladder Pain and Frequency

The innervation of the bladder has been described in detail elsewhere. Briefly: The bladder is innervated by both the sympathetics and the

parasympathetics by way of the hypogastric ganglia. The sympathetics are inhibitory to the detrusor vesicae and motor to the trigone and internal sphincter. The parasympathetics are inhibitory to the internal sphincter and motor to the detrusor. In addition, there is the pudic pathway, which is motor to the external sphincter and sensory to the posterior urethra. Pain impulses reach the central nervous system via both the sympathetic and parasympathetic pathways, but principally by the latter. With the exception of the inconsiderable filaments which join the hypogastric ganglia direct from the sacral paravertebral sympathetic chains, the great majority of its sympathetic nerves reach the bladder by way of the presacral nerve (superior hypogastric plexus).

Attempts to relieve pain arising in the pelvis by sympathetic surgery date from the work of Jaboulay, who, in 1898, attempted to cut the rami communicantes of the sympathetic chain by a retrorectal approach. Cotté, in 1925, first employed presacral neurectomy for the relief of pelvic pain, and reported many instances of relief of pain by this means in gynecological cases. In 1926, Pieri successfully employed presacral neurectomy, with sectioning of the sacral rami communicantes and dividing of the sacral sympathetic chains at the level of the first sacral segment, for the relief of pain in vesical tuberculosis. Learmonth (1930) applied presacral neurectomy to paralytic bladders. Recent periodical literature contains many reports of good results through presacral neurectomy in the relief of intractable vesical pain and frequency.

Presacral neurectomy is indicated (1) in certain cases of localized submucous fibrosis, tuberculous cystitis, inoperable carcinoma of the prostate or bladder, and other lesions producing intractable vesical pain and spasm; (2) in selected cases of tabetic bladder and vesical paralysis due to cord injuries. If there is a complete transverse lesion of the cord with funneling of the vesical neck, presacral neurectomy is contraindicated; but in cases with retention and overflow incontinence, where there is a tight external sphincter and adequate renal function, and where the lesions seem mainly to be in the parasympathetic pathway, relief may be expected. In the more successful cases the residual urine is reduced and the patient is able to void with greater ease. In paralytic bladders there is also relief of the constant aggravating pain to which the patient has been subject.

Technic of Presacral Neurectomy. The following is the technic of Learmonth: Under spinal anesthesia, and with the patient in the Trendelenburg position, a left paramedian incision is made, a third of the

incision being above the umbilicus and two thirds below. The intestines are packed off so as to disclose the bifurcation of the aorta, the two common iliac arteries, the left common iliac vein, part of the anterior surface of the fifth lumbar vertebrae, and the promontory of the sacrum. The peritoneal covering of the promontory is incised longitudinally to the upper limit of the exposure. Each lip of the peritoneal incision is then carefully retracted, thus excluding the inferior hemorrhoidal artery from the field. In lean subjects it is usually possible to identify the strands of the presacral nerve before the peritoneum is incised; in fat patients it is better to work from the left side to the right. A strand of the presacral nerve can usually be identified as it crosses the left common iliac vein. This strand is then placed on a blunt hook, and as further strands are identified and dissected free—first toward the median line and then toward the right common iliac artery—they are in turn placed on the hook. At the conclusion of the dissection, the common iliac arteries and the left common iliac vein should be denuded of nerve fibers. The nerve is now divided between ligatures, as high up as possible. The peripheral end is raised by blunt dissection with a cotton pledget, and any communicating fibers from the lower left lumbar ganglia severed. Each hypogastric nerve is clamped and divided proximal to the clamp as soon as it is encountered. The segment of each hypogastric nerve may then be removed and the clamps later replaced by ligatures. It is seldom necessary to place ligatures upon vessels in the tissues from which the nerves have been removed.

The wound in the posterior peritoneum is closed with fine catgut, and the abdominal wound in the usual manner.

Resection of Superior Hypogastric Plexus and Sacral Ganglions. The literature has shown that simple excision of the superior hypogastric plexus for the relief of vesical pain does not suffice in all cases. In selected cases, therefore, Schroeder and Cumming recommend excision of the superior hypogastric plexus and exeresis of the lateral sacral sympathetic chains. They have recently published a series of 12 cases of vesical tuberculosis and interstitial cystitis in which significant and lasting improvement was obtained through this operation. Their technic is similar to that of Cotté and Learmonth, but they divide the sacral sympathetic chain at the level of the first sacral segment, as originally advocated by Pieri. "The proximal end of the distal segment is then grasped with a hemostat and the instrument is rotated, the nerve being wound on the clamp and at the same time the chain being gradually freed

with a blunt instrument from all its attachments to or below the third sacral segment."

Surgery for Incontinence of Urine

Incontinence of urine is a most distressing lesion in both men and women. In numerous instances we have had success in relieving this condition, whether due to congenital or acquired factors, by the use of two procedures described by Lowsley in 1929 and 1936 respectively. We have had good results with both methods, but of late the second operation—a plication procedure—has been the operation of choice.

Repair of Vesical Orifice for Cure of Incontinence (Lowsley). This operation consists in diverting the urine by a suprapubic cystostomy, dissecting free the top of the urethra, taking a wedge-shaped section of tissue from the roof of the vesical orifice (and the anterior of the prostate in the male), and thereafter reconstructing the urethra over a small catheter by chromic catgut sutures (Figs. 261 and 262).

Lowsley-Hunt Plication Operation for Incontinence of Urine and Feces in the Male. The patient is placed in the lithotomy position, and a sound is inserted into the urethra (No. 19-F. in adults, a much smaller one in children). A median or Y-shaped incision is made in the perineum and deepened through the fat and Colles' fascia, exposing the bulbocavernosus muscle, which is then dissected free on all sides. Chromic ribbon gut, studded with an atraumatic needle, is inserted well down on the lateral surface of the muscle. It is then fixed in a similar manner on the opposite side, pulled tightly across the posterior surface, and tied in a square knot. This is repeated at two other points over the bulbocavernosus muscle, resulting in a rather firm plication of the entire muscle. The object is to produce an elastic narrowing of the bulbous portion of the urethra so that the patient must use considerable force to empty his bladder.

The sound is removed and the fascia and skin closed with plain catgut and fixation sutures respectively.

Sometimes incontinence of feces also occurs, in which case the rectum can be plicated with ribbon gut, as shown in figures 263 and 264. Both the urethral and rectal plications may be accomplished through the one incision in the perineum.

Postoperative Care. The patient must usually be catheterized every 8 hours for 2 or 3 days after this operation. He then begins to void without aid. He is instructed to void every 2 or 3 hours while up and

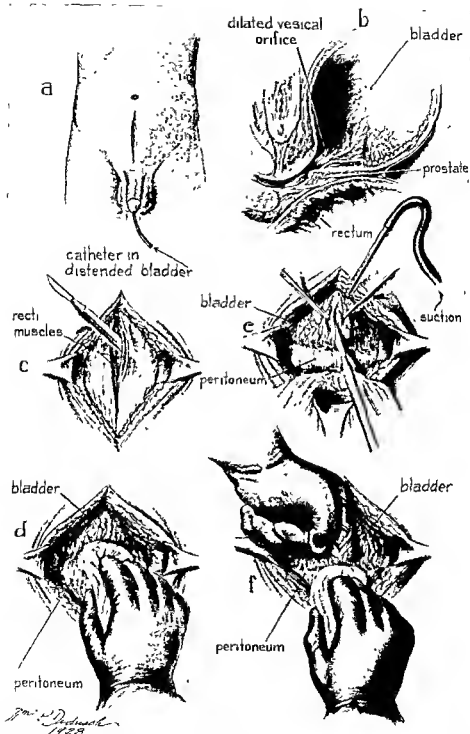
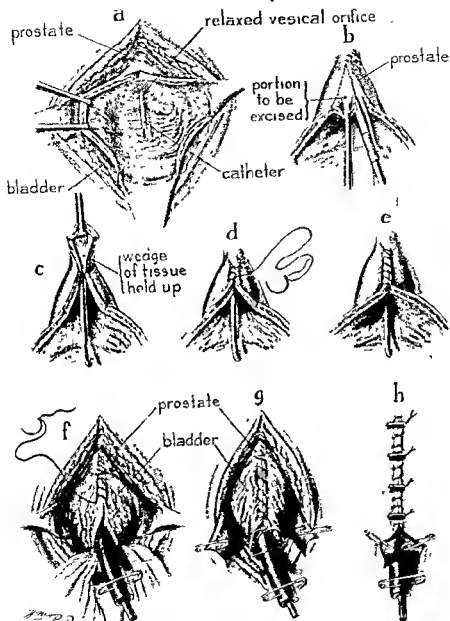


FIG. 261. Repair of vesical orifice for cure of incontinence. (a) Median incision. (b) Sagittal section showing relaxed vesical orifice. (c) The recti muscles are separated and (d) the peritoneum stripped from the bladder. (e) The bladder incised and fluid removed by suction. (f) Further stripping of the peritoneum from the bladder.



Wm. H. Dudley
1928

(a) The bladder is opened, moved from (d, e) The bladder skin closure.

about, and to use suprapubic pressure, if necessary, to empty the bladder completely.

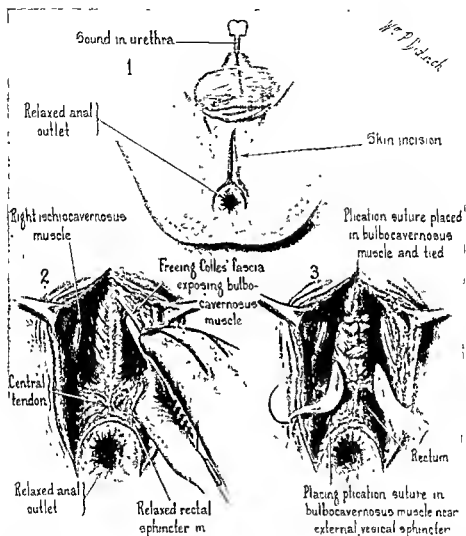
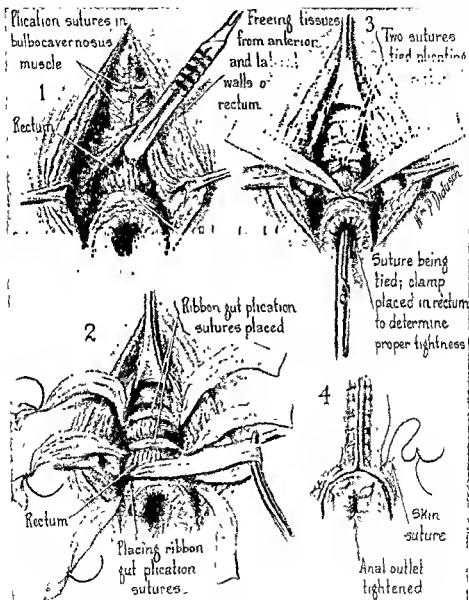


FIG. 263. Lowsley-Hunt plication operation for incontinence of urine and feces in the male. (1) Skin incision. (2) Exposing the bulbocavernosus muscle and the wall of the rectum; dissecting free the bulbocavernosus. (3) Plicating the bulbocavernosus muscle with ribbon gut.

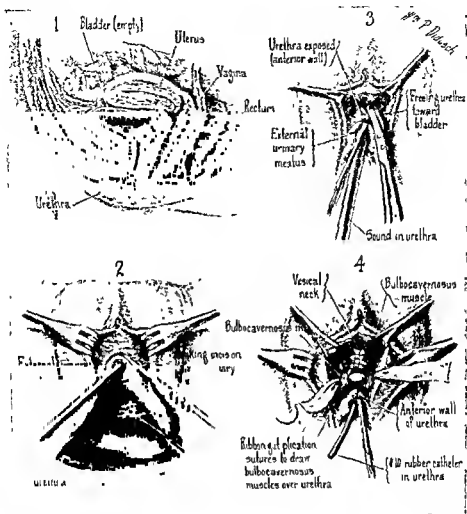
Plication Operation for Incontinence of Urine in the Female. The procedure of choice depends on the situation which the surgeon encounters. If the urethra is very large and patulous, and the patient is entirely incontinent, the ventral surface of the urethra is plicated with chromic ribbon gut over a No. 10-F. baby catheter, which is left in position for 2

or 3 days, as shown in figures 265 and 266. If, on the other hand, the patient merely loses a few drops of urine on coughing or other violent



muscular activity, encircling the urethra with a piece of ribbon gut and tying it snugly will frequently be all that is necessary to effect a cure.

Fibrous tissue replaces the ribbon gut, as shown in our animal experiments.

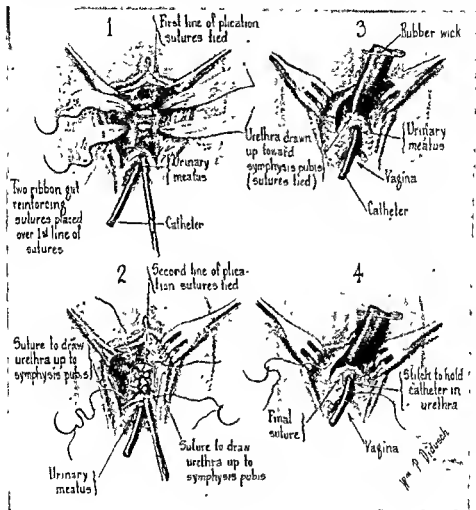


(1) Sagittal
(2) With a
The anterior
ut sutures are

Kelly Plication Method. We have also had success with the Kelly plication operation. We substitute chromic ribbon gut for the No. 0 chromic catgut, however, and plicate the roof of the urethra instead of the floor.

With the patient in the lithotomy position, and a Pezzer catheter in

the bladder, the perineum is depressed and the anterior vaginal wall stretched by the application of clamps to the cervix and lower urethral wall. The head of the catheter is pulled down until it reaches the internal urethral orifice. The position of the bladder neck is readily determined



by moving the catheter to and fro with its head pressed against the urethra. The sphincter will lie just in front of the catheter's bulb and the operator will be able to palpate it through the front wall of the vagina. At this point a two-inch incision is made in the vaginal wall

down to the vesical wall, the vaginal mucous membrane grasped with Allis clamps, and the mucosa loosened and lifted up so as to expose the bladder neck.

Two or three superimposed mattress sutures of chromic ribbon gut, on a fine curved and rounded needle, are set in the sphincter region, the needle being introduced a half inch from the median line at each side. This folds back the muscle for about an inch. A continuous lock-stitch of chromic ribbon gut is then set in so as to fold over the wall of the bladder and posterior urethra, and cover the mattress sutures, thus relieving any tension. The abdominal wall is closed in the usual manner. If the operation has been properly performed, the catheter will meet with resistance when withdrawn.

Muscle-transplantation Procedures for Formation of an Artificial Sphincter. Different operators have substituted some other muscle for the destroyed, missing, or incompetent sphincter, with varying success.

Deming (1927) looped the proximal end of the gracilis muscle about the bladder neck in a young woman who had congenital epispadias with urinary incontinence.

Martius (1928) proposed the use of the bulbocavernosus and ischio-cavernosus muscles for the formation of an artificial sphincter. The muscle mass is mobilized, detached at its anterior end and brought across beneath the bladder neck, and the end of the muscle attached to the opposite side with sutures. Great care is necessary to prevent injury to the vessels and nerves at the points where they enter the posterior and outer aspects of the transplant; otherwise, nutrition to the parts would be cut off and the operation doomed to failure.

Goehell, Frangenheim, Stoeckel, and others have utilized the pyramidalis, with strips of fascia from the rectus. The so-called Goebell-Stoeckel operation consists of an initial dissection by which the bladder neck is completely freed from the surrounding tissues. The attachments of the pyramidalis muscles to the pubis are left intact, but a strip is taken from each muscle, passed down the urethra and vesical neck, and attached to the periosteum of the pubic ramus of the opposite side. If the pyramidalis muscles are poorly developed or missing (an occasional happening), strips can be obtained from the rectus abdominis muscles. This operation was originally done in two stages, but it is now considered better to perform the entire procedure at one time, if possible. The operative wound should be made upon the abdominal surface, avoiding opening of the vaginal mucous membrane, with the risk of infection of the suprapubic area. After the muscle strips have

been attached to the pubic rami, the abdominal incision is closed about a catheter, which is left in the bladder for several days, thus avoiding the passage of urine over the operative site until primary healing has had time to take place.

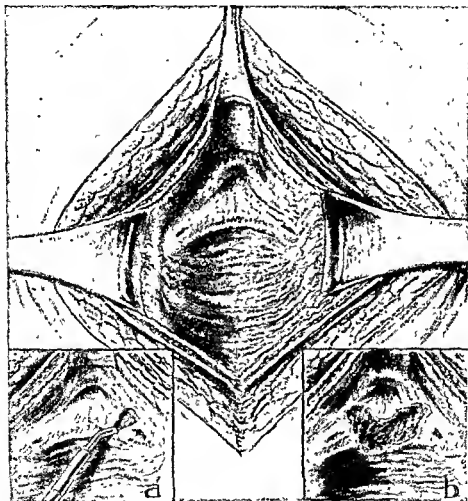


FIG. 267. Removing obstructive portion of hypertrophied trigone with the electrocautery. The bladder opened, showing the hypertrophied trigone with pouch behind it. (a) Excising the trigone with the cautery. (b) Condition of the trigone after use of the cautery.

Excision of Hypertrophied Trigone

Under certain conditions the trigonum vesicae becomes hypertrophied, and it may be desirable, for the relief of symptoms, to excise it (*Hypertrophy of the Trigone*, p. 1065). In figure 267 is shown such a condition and the method employed for relieving it.

Fulguration and Resection of Vesical Neoplasms

SIMPLE FULGURATION OF BENIGN PAPILLOMA

Since its introduction by Beer, in 1910, fulguration has been the surgeon's mainstay in the destruction of benign vesical tumors, whether single or multiple. It is important, however, that the diagnosis be fully established, for fulguration alone has not been found satisfactory for malignant neoplasms. If the growth is fairly large, or if there are multiple growths, it is usually better to do an open operation.

Technic. The technic is comparatively simple. Through an operating cystoscope a properly insulated wire conveys an electrode which is connected with the Oudin resonator. The electrode is passed until its tip invaginates the surface of the papillomatous mass. As the current is turned on and the cauterization begun, bubbles are seen rising through the fluid used to distend the bladder. Soon a blanching of the tissues is noticeable. This is due to dehydration, which destroys the vitality of the tumor tissue. The lesion is burned away until it presents a white mass—considerable judgment being required of the operator to determine exactly how deep the cauterization may be carried without perforating the bladder wall. The cauterized tissue later sloughs off and is evacuated with the urine.

TREATMENT OF PAPILLOMATOSIS BY RESECTION AND CAUTERIZATION
WITH PHENOL AND ALCOHOL

Although Beer's method of fulguration (by the transurethral route or through a cystostomy incision) has been the standard method of treatment for benign papilloma for over three decades, the results have been far from satisfactory, recurrences being distressingly frequent.

On the theory that vesical papillomatosis is due to infection by a filterable virus (see p. 1051), Kirwin has recently carried out complete removal of the papillary growth or growths with the cutting current (instead of the usual fulguration technic), followed by cauterization with phenol and alcohol. The results by this new method, reported by Kirwin early in 1943, have been definitely encouraging.

Technic. Through a midline suprapubic incision the bladder is exposed and opened with the straight wire electrode. The edges of the incision are protected by gauze as an additional precaution against the spread of an infectious condition. The neoplastic tissue is removed

down to the muscularis with the wire loop electrode, the exposed base then being cauterized by the application of the ball electrode. If more than one tumor is present, each growth is treated in a similar manner. A solution of 50 per cent phenol in glycerine is next applied not only to the areas from which the growths have been removed, but also to the mucosa of the ureteral orifices, prostatic urethra, cut edges of the bladder, and the bladder cavity throughout, thus sterilizing all possible sites of recurrence. This is followed by the application of 95 per cent alcohol when the phenol has been in contact with the mucosa for about three minutes. A drainage tube is inserted in the bladder and the bladder incision closed around it. A drain is placed in the space of Retzius and the suprapubic wound closed about the drain in the usual manner.

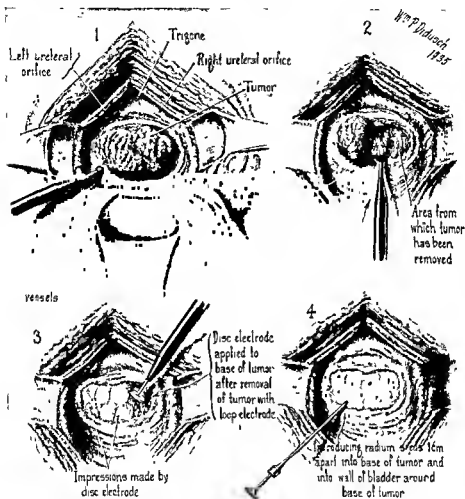
RESECTION-AND-IRRADIATION TREATMENT OF MALIGNANT TUMORS

Closed Method. Small papillary carcinomas, with little infiltration of the bladder wall, often can be treated by transurethral electrocoagulation of the exuberant portion of the growth, followed by the implantation of radon seeds. We have found the Kirwin resectoscope particularly well adapted for removing the exuberant portion of the growth, because its electrode is protected by a fenestra, minimizing the danger of penetrating the wall. If a resectoscope is not available, simple fulguration may be employed for removing the body of the tumor. The important feature is the removal of the projecting mass, so that the base may be fully exposed for radon implantation.

Kirwin has designed an instrument which facilitates both the inspection and measurement of the tumor, permitting correct estimation of the amount of radon required to irradiate the base after the mass of overgrowth has been removed by the resectoscope or fulguration; also an implanter, by means of which radon seeds may easily be introduced into the tumor by either the open or the endoscopic route (*Radium and Roentgen-Ray Therapy of Bladder Tumors*, p. 1750).

Open Operation (Ball-Loop-Disc Method). Large carcinomas that are not surgically removable should be treated by excision of the exuberant portion of the tumor with the loop electrode, through a suprapubic incision, followed by the implantation of radon seeds. Three different electrodes are employed in carrying out this technic. The ball electrode is first applied to the bladder wall surrounding the tumor, to seal off the vessels. The entire tumor mass is then removed with the loop

electrode. After the overgrowth has been excised, the disc electrode is applied to the base of the tumor, to control any hemorrhage that may be present. When the entire site has been thoroughly cauterized, radon



seeds. (4) The entire tumor mass is de is then used to cauterize the surface. the base of the tumor and the sur-

seeds are implanted 1 cm. apart into the base of the tumor and into the wall of the bladder around the base, so as to take care of any in-

filtration which may have taken place in the muscular wall of the bladder.

Postoperative Care and Complications Following Surgery of the Bladder

Immediate Postoperative Care. The immediate postoperative care consists in keeping the patient warm and quiet. If he has had spinal anesthesia, his head must be kept lowered for 6 or 7 hours. His pulse,

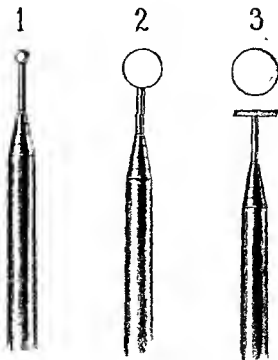


FIG. 269. The three electrodes used in the ball-loop-disc method of fulgurating bladder tumors.

respirations, and temperature must be carefully observed and the secretions examined for undue bleeding.

Complications. *Shock* is the complication most feared after any operation, including those upon the bladder. This is caused by loss of blood or pain. If there is moderate loss of blood, the patient should receive intravenous injections of glucose (50 per cent) in large quantities. If considerable blood is lost, it should be replaced by whole blood transfusion. *Cardiac failure* is relieved by stimulation and by placing the patient in an oxygen tent. *Pneumonia*, as a postoperative complica-

tion, is less frequent now than when general anesthesia was in common use. In the occasional instances when it does occur the patient is benefited by being placed in an oxygen tent and given sulfapyridine by mouth.

Suction Drainage. Double Suction Tube. In the Brady Foundation, patients are kept clean, dry, and comfortable, and afforded perfect drainage, by means of the double suction tube and the use of the suprapubic suction cup.



FIG. 270. Suprapubic suction apparatus used at the Brady Foundation, at the New York Hospital. The suprapubic tube is connected to a long piece of rubber tubing, which in turn is attached to a metal right-angle tube inserted in a two-holed rubber cork in a drainage bottle attached to the frame of the bed. A second long piece of rubber tubing has one end attached to the wall suction and the other to a shorter metal tube inserted in the rubber cork. The exhaust tube, the one connected to the suction, passes through the cork for a distance of 1 inch; the intake tube, the one connected to the double suction tube, for about 5 inches. This difference in length is to prevent bursting bubbles of urine being drawn into the

The cystostomy tube is connected to a long piece of rubber tubing, which, in turn, is attached to a metal right-angle tube inserted in a two-holed rubber cork in a drainage bottle attached to the frame of the bed. A second long piece of rubber tubing has one end attached to the wall suction and the other to a shorter metal tube inserted in the rubber cork. The exhaust tube, the one connected to the suction, passes through the cork for a distance of 1 inch; the intake tube, the one connected to the double suction tube, for about 5 inches. This difference in length is to prevent bursting bubbles of urine being drawn into the

exhaust tube. Suction is obtained by gently pushing the lever of the wall suction to get the desired pressure.

The double suction tube is irrigated daily, at the same time the dressings are changed. The inner tube is cleansed and replaced whenever it appears to be blocked. The drainage bottle is changed every 12 hours, and cleansed and sterilized with a germicidal solution. The rubber tubing from the bottle to the patient and the metal connecting-tubes are removed daily and replaced by clean, sterile tubing.

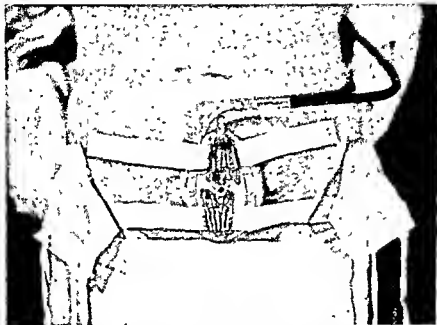


FIG. 271. Suprapubic suction cup. Showing the cup attached to the patient. Elastic bands are placed about the safety-pins to provide tension and prevent abdominal movements from loosening the cup.

Suprapubic Suction Cup. For several years we have been using a simple and most effective drainage device, which was originally suggested to us by Mr. Leo Savolly, an orderly at the New York Hospital. This suprapubic suction cup and its method of attachment to the patient are shown in figures 271 and 272. This device is used to bridge the period between the removal of the drainage tube and the healing of the sinus.

The cup consists of a flat, hollowed-out rubber sponge. Inside the rim of the cup is a turn of small rubber tubing with several holes. One end of this tubing is sealed, while the other extends out the side of the cup and is attached to the drainage bottle. There are two vents in the

collecting-chamber of the cup. No actual suction is made on the sinus, the urine being merely drawn off as it wells up into the cup.

After the double suction tube has been removed, the suction cup is placed on the abdomen directly over the suprapubic sinus, so that the fistula is in the center of the hollowed-out portion of the cup. It is held in place by two adhesive straps or by the use of adhesive straps and rubber bands. Over the cup is placed a gauze pad, held in place by

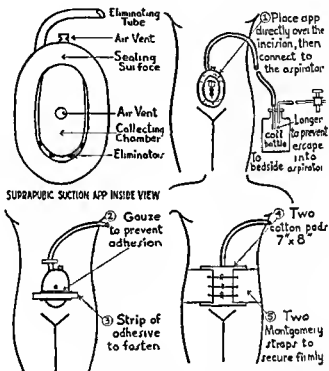


FIG. 272. Suprapubic suction cup. Schematic drawing of cup and method of attaching it to the patient.

Montgomery straps. The cup is connected to the suction apparatus in the same manner as the double suction tube.

This device is simple to manage, saves gauze, prevents an ammoniacal odor in the ward, and, most important of all, makes the patient feel much better. Urine does not run over him and soak the linen, so that he is not subjected to excoriation and decubitus of his back from lying in a puddle of urine, and the laundry bill is reduced to the daily change of linen.

Stedman Induction Motor Suction Pump. The induction motor suction pump, recently devised by Dr. Harold E. Stedman, at the New York

Hospital, is particularly useful in hospitals with only a few urological cases, where the installation of an elaborate vacuum system would be impractical and too expensive.

The pump is 6 inches long, $4\frac{1}{2}$ inches wide, and 6 inches high, and weighs only 6 pounds (Fig. 273). It consists of a substantial cast aluminum frame, an electromagnet, a copper rotor, and a piston and cylinder. The pump is self-starting, non-reversible, noiseless, and creates no radio interference. It is self-regulating, adjusting its speed to the

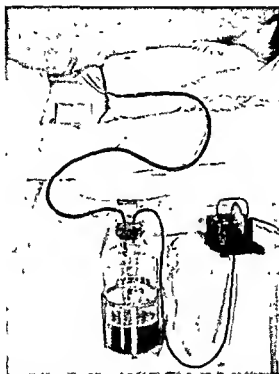


FIG. 273. Stedman induction motor suction pump. Complete set-up, showing patient with double suction tube, collecting-bottle, and Stedman suction pump in use. The dressings have been removed from the suprapubic wound. (Courtesy of Dr. Harold E. Stedman.)

amount of suction. It operates on alternating current only, 50 and 60 cycles, and can be supplied for 110 and 220 volts. The current consumption is less than 20 watts per hour when operating on the rated voltage. Due to its slow speed and adequate lubricating system, it will run continuously with very little attention and will produce sufficient vacuum to elevate a column of water 7 feet. It can be used on two or even more patients at the same time.

The pump can be attached to the double suction tube, or to the suprapubic suction cup, or to a Pezzer or wing-tip catheter.

Forcing of Fluids. Cystostomy is most often done for the purpose of drainage (*i.e.*, as a preliminary to prostatectomy). In such cases fluids are always forced.

As a rule, the amount of fluid to be taken daily is 3,000 cc. for all urological patients with the exception of prostatic patients, who are usually given from 3,000 to 4,000 cc. An intelligent adult patient will usually cooperate readily when the necessity of the forcing of fluids is explained to him. With some patients, persuasion or patient persistence is necessary. Specially trained urological nurses are of the greatest aid in these cases. The nurse estimates the amount her patient must drink each hour in order to receive his daily requirement, making allowance for the fact that he drinks less at night. Fluids should be provided in whatever form is best tolerated by the patient. Some patients prefer ice-water, cool water, or warm water, while others will drink water that is flavored with fruit juices.

If fluids are administered by rectum, it should be noted whether or not the entire amount is retained; if not, an estimate should be made of the loss. The deficiency may then be made up by hypodermoclysis or infusion.

Charting Fluid Intake and Output. The following applies not only to bladder cases, but to the majority of urological cases.

The intake of fluids and the amount of urine excreted are measured and recorded in accordance with the practice of the particular hospital. The following is the practice in our service at the New York Hospital.

Measuring Fluid Intake. (1) The nurse measures the fluid intake when the patient is on "measured intake."

(2) When a patient is put on "measured intake" a shipping-tag is placed about the neck of the carafe; on this is written the name of the patient and the amount of fluid he is to receive:

John Miller Force Fluids	or	John Miller Limit Fluids
4000 cc.		1200 cc.

(3) The total fluid intake for a patient on "measured intake" is apportioned by the nurse in charge. A suggested plan for urological patients is:

Diet fluids	.	½ of total fluid intake
Water		
7 a m. to 11 a m.	.	¼ of total fluid intake
11 a m. to 3 p m.	..	¼ of total fluid intake
3 p m. to 7 p m.	. ..	¼ of total fluid intake
7 p m. to 7 a m.	¼ of total fluid intake

If the amount of fluid ingested is increased or decreased during any one period, it is subtracted from or added to the amount in the following period, and the amount altered accordingly on the fluid chart by the person making the change.

(4) The floor clerk or nurse makes out the fluid chart and gives it to the dietitian before 3 p.m. of the previous day. The nurse in charge

TABLE VI

Fluid chart

Pavilion: Urology.

DATE: February 1, 1943

FLUID RECEIVED, 24 HOURS	TIME	NAME											
		Jones, John		Green, Jo		Smith, Sam		Doe, Mary		Henry, Ida			
		Required and served	Taken	Re-quired and served	Taken	Re-quired and served	Taken	Re-quired and served	Taken	Re-quired and served	Taken		
Diet fluids	Breakfast	200	200										
	10 a m	200	200										
	Dinner	400	400										
	3 p m	200	200										
	Supper	200	200										
	8 p m.	200	200										
Total			1400										
Water	7 a m -11 a.m.	Required	Served	Taken	Required	Served	Taken	Required	Served	Taken	Required	Served	Taken
	11 a m.- 3 p m.	650		500									
	3 p.m.- 7 p m.	800		650									
	7 p m - 7 a.m.	800		600									
		850		850									
Total				2600									

inserts the amounts planned for the water intake during the various periods of the day.

(5) The dietitian records on the fluid chart the amount of fluid planned for each meal and returns the chart to the nurse in charge before 7 a.m. of the day it is to be used. This sheet is posted in the pantry.

(6) Before the meal trays are returned to the pantry, the nurse who is posted for "intakes" inspects the trays of the patients on "measured intake" and urges those on forced fluids to drink the fluids. She records the fluids for those patients who have taken the entire amount. When

the trays are taken to the kitchen, the nurse estimates the remaining fluids on each tray and records the amounts on the fluid charts.

(7) The total amount of diet fluids and the total amount of water for the day and night are charted on the nurse's notes in the column *Diet and Fluid Intake* in blue ink for day and red ink for night. This charting is done at the end of the period, *i.e.*, 7 a.m. to 7 p.m., 7 p.m.

TABLE VII

Urine output

TIME: 7 p.m.-7 a.m. or 7 a.m.-7 p.m.

DATE: February 1, 1943

NAME	7	8	9	10	11	12	1	2	3	4	5	6	7	DRAINAGE	TOTAL	REACTION	DEVECA- TION
	cc.		cc.	cc.	cc.	cc.	cc.	cc.	cc.		cc.	cc.		cc.	cc.		
Jones, John...	200		350	100			500		200			400			1750	6.5	0
Green, Henry.													2500†		2500	7	1
Smith, Mary..	50					50			800*						100‡ 800‡ 900	5.5	0
Miller, Jane...	100				300			100			275		400‡		1175	6.0	$\frac{E}{1}$
Black, Joe ..	200			400				100			325		500§		1525	6.5	1

* Catheterization.

† Suprapubic.

‡ Urethral catheter right

§ Nephrostomy

¶ Voiding.

|| Catheterize.

to 7 a.m., or at 12 midnight, depending upon the requirements of the particular service.

Example:

	cc.
7 a.m. to 7 p.m.	
Diet fluids	600
Water	3000
Total Fluids	3600
7 p.m. to 7 a.m.	
Diet fluids.	400
Water	600
Total Fluids	1000

"Total fluids for 24 hours 4600 cc." is charted on the temperature sheet in the space designated.

Table VI is a sample of the fluid chart kept in the pantry (these notations are copied upon the patient's chart).

Measuring Fluid Output. Under *Fluid Output* must be recorded not only all urine obtained by voiding or catheterization but all that is passed from the body by drainage tubes. If urine escapes into the dressings or alongside a retention catheter, the amount so lost must be carefully estimated. The patient must not be permitted to go to the toilet, even if able, so long as his condition demands the keeping of records of his daily fluid output. Fluid lost by vomiting should also be measured and noted in the nurse's notes. After each voiding the urine is carefully measured and the amount promptly recorded in the utility room on a convenient chart, as in Table VII.

The only difference between the day and night charts is that, on the night chart, there is an additional column for the reaction of the urine, which is obtained by testing with nitrazine paper every morning.

The data from these charts are copied upon the patient's chart by the nurse at 7 a.m. and 7 p.m.

The nurse in charge must always watch carefully to see that each patient has sufficient urinary drainage. This is not difficult even in a large and busy pavilion, provided the entire staff understands that the fluid output affects these patients to the point of recovery or complete collapse which may result in death. The nurse or orderly must, therefore, be alert in noting the first sign of diminished output from any patient, and must report the same promptly to the nurse in charge.

Follow-Up of Patients After Bladder Surgery

All patients who have had an operation upon the bladder are urged to return regularly for check-up examinations.

As has been repeatedly emphasized, any patient who has had a vesical tumor must be kept under surveillance more or less for the remainder of his life. If the gravity of the situation is properly represented to the patient, he will usually be willing to undergo the inconvenience or actual distress of a cystoscopic examination at comparatively frequent intervals, which can gradually be lengthened if there is no sign of recurrence.

In calculus cases, the stone is analyzed, and, depending upon whether it is an alkaline or an acid calculus, the patient is placed upon an acid ash diet and given acidifying drugs, or upon an alkaline ash diet and given an alkaline water and alkaline drug, in order to keep the urine

constantly acid or alkaline (as the case may demand) to prevent further formation of calculi. He is also given nitrazine paper to test the reaction of his urine daily. Such a regimen requires a check-up at regular intervals.

B. NON-OPERATIVE TREATMENT OF THE BLADDER

Bladder Irrigations and Instillations

One of the most helpful measures for relieving vesical irritation is irrigation with various solutions. The simplest of these are normal saline solution and boric acid, 2 per cent. Good antiseptics for vesical lavage are rivanol dextrose, 1:8,000, which is especially useful in chronic colon bacilluria, being both antiseptic and soothing; acriflavine, 1:5,000 or 1:10,000 potassium permanganate, 1:8,000 or 1:10,000. Silver nitrate, 1:10,000 is useful in hemorrhage of the bladder, but should never be used, in any strength, in cases of vesical tuberculosis because of its irritative qualities. Keyes has shown that in long-continued hemorrhage, sodium citrate, 1:8000 will prevent the formation of impassable clots.

In alkaline encrusted cystitis, we have had good results with a solution containing magnesium oxide anhydrous and citric acid, the formula for which is given on p. 1013.

The irrigating solution should be given at a temperature of 100 to 110°F., depending on the tolerance of the individual bladder. Care should be taken not to hold the container too high, if the gravity method is used, for too great pressure may set up inflammation of the epididynes. Irrigation through a soft rubber catheter is generally preferable. The patient should void the injected fluid naturally, if possible. The bladder irrigations should be given daily at first and then two or three times a week.

Whenever a patient has an indwelling urethral catheter, this must be irrigated once in 24 hours to prevent the formation of urates. Boric acid in a 2 per cent solution is usually employed unless active bleeding or considerable infection is present. When there is bleeding or severe bladder infection, much more frequent irrigation is necessary. These patients are usually put on intermittent bladder irrigation. Normal saline or silver nitrate solution, 1:10,000 is usually used when bleeding is present; saline or potassium permanganate solution, 1:10,000 when there is severe infection.

In very acute cases the instillation and retention of an ounce or two of novocaine borate, 2 per cent will give temporary relief. Instillations of acetic acid, 1 per cent have been found effectual in infections due to

the pyocyanus bacillus, and phosphoric acid, 1 per cent in cases of staphylococcal infections which produce a strongly alkaline urine.

Intermittent Bladder Irrigation

Intermittent bladder irrigation is employed (1) when it is advisable to cleanse the bladder frequently, (2) to help prevent bleeding and clot-formation, (3) to relieve inflammation and congestion.

The apparatus used by us consists of a 700-cc. Kelly irrigating flask with a piece of rubber tubing 4 feet long leading to the stem of a Y-tube. From one prong of the latter leads a piece of rubber tubing $1\frac{1}{2}$ feet long fitted with a straight glass connecting-tube which is connected to the patient's indwelling catheter. From the other prong a piece of tubing 2 feet long leads to the drainage bottle at the patient's bedside.

When irrigating, 25 to 50 cc. of the desired solution is allowed to flow into the bladder at a time, the irrigation being continued until the return is clear (usually 3 or 4 times). About 50 cc. of solution is allowed to remain in the bladder between irrigations by clamping off both the inflow and outflow.

In order to compute the patient's urinary output when intermittent irrigation is being given, a very accurate recording must be kept of the amount of solution put into the flask. The urinary output is computed as follows: The amount of solution that goes out through the irrigating system into the drainage bottle is the *total output*. The difference between the amount of irrigating fluid used and the total output represents the *urinary output*.

Gradual Decompression of the Bladder

Decompression of the chronically distended bladder is a maneuver attended with the greatest of danger if it is not done intelligently. If the intravesical pressure in such a bladder is suddenly reduced, by complete emptying, serious congestion of the bladder, kidneys, or both, with grave or even fatal consequences, may result.

There are two methods of decompression in vogue. One is to remove a moderate amount of urine and let the bladder refill, or to remove it all and immediately replace half the amount and let the urine collect again. The other method is to keep a certain amount of pressure within the bladder by means of a decompression apparatus that permits the urine to run out of the bladder very slowly but continuously.

It is our custom to reduce the intravesical pressure gradually, first by

intermittent catheterization, replacing 50 per cent of the amount removed, and, finally, by maintaining continuous outflow by means of a **A** tube connected with a reservoir the height of which is adjusted at a level permitting the urine to run out of the bladder freely. If the urine spills over the arch in the **A** tube when the patient breathes or coughs, the apparatus is working satisfactorily.

A very simple method that can be carried out in any sick-room is that advocated by Hamer, of Indianapolis, namely, attaching the end of the tube leading from the catheter to a bottle on a stand which is so placed that the tube starts at 2 feet above the bladder level, and lowering it 2 or 3 inches a day until the urine is flowing quite freely.

The results of gradual decompression in obstructed cases warrant a continuation of these methods, as one now rarely sees the cases of uremia which were altogether too common in the earlier days of vesical and prostatic surgery.

Automatic Tidal Drainage of the Bladder

Tidal drainage of the bladder was introduced by Donald Munro, of Boston, in 1935. Together with Joseph Hahn, he devised an apparatus which distended the bladder to a suitable degree with antiseptic solution and then automatically emptied it. The Munro-Hahn irrigator was designed preeminently for use in abnormal bladders resulting from injury or disease of the spinal cord, but was apparently too complicated for wide use in urological cases occurring independently of such injury. To Munro, however, must go the credit for establishing the value of the method beyond doubt. He classified "cord bladders" into certain recognizable groups, or stages (the atonic bladder, the autonomous bladder, the hypertonic bladder), and was able to show that, with tidal drainage, the incidence of urinary infection dropped from 73 to 15 per cent.

Many modifications of Munro's original apparatus have been devised, some of which have a very general application while a few are limited to use in special cases (Hyams and Buchtel, Lawrie and Nathan, Bellis, Myers, MacNeill and Bowler, W. G. Hayward, and others). With the designing of simpler irrigators, tidal drainage of the urinary bladder has become a valuable and dependable addition to the urologist's armamentarium.

Apparatus for Tidal Drainage. The apparatus used by us is essentially similar to that devised by Lawrie and Nathan. It consists of a 700-cc. Kelly irrigating flask with a piece of rubber tubing 8 inches long (Hoffman screw clamp) leading from the flask to a Murphy drip bulb (open vent). A second piece of rubber tubing, 16 inches long, leads from the

Murphy drip bulb to one prong of a glass Y connecting-link. To the other prong leads a piece of rubber tubing 6 feet long, which connects with the drainage bottle at the patient's bedside. The straight arm of the Y tube connects with 3 feet of rubber tubing with a straight glass connecting-link, which is connected to the patient's catheter. The catheter should be at least No. 16-F., and should be changed weekly if the drainage is to continue over a period of weeks.

Tidal drainage imitates the natural physiology of the bladder. We quote from Lawrie and Nathan:

The bladder is filled at a slow-drip rate; as it fills, the intravesical pressure rises gradually until it reaches the level of the siphon-tube. Siphonage then begins and continues until, when the bladder is empty, the siphon-tube is filled by air entering through the side-piece of the drip-bulb. Siphonage then ceases, and the bladder starts to fill again. At this moment there should be no residual urine in the bladder, a fact which may be confirmed by disconnecting the catheter. This cycle continues as long as there is fluid in the reservoir.

The maximal negative pressure acting on the bladder is equal to the vertical height of the symphysis pubis above the Y-piece; we have found 7 inches a suitable height. The maximal intravesical pressure never rises above the vertical height of the apex of the siphon-tube above the symphysis pubis. The exact height depends on the patient's comfort and the condition under treatment. A height of about 7 inches is correct for the normal bladder, and 10 inches or more for a hypertonic bladder. It is impossible for the apparatus to distend the bladder to a greater pressure than the height of the siphon-tube. A suitable rate for the flow of antiseptic solution is 60 drops a minute. Since it is in contact with the vesical mucosa for at least 23 hours out of the 24, a mild solution should be used.

Irrigating Solutions. The irrigating solutions most frequently used are a 1.5 or 2.0 per cent solution of boric acid, and acriflavine, 1:5,000. Other solutions that have been found safe and useful are: normal saline, oxycyanide of mercury, 1:8,000, potassium permanganate, 1:30,000, a 3.0 per cent solution of sodium citrate (when clots are likely to form), and a 0.5 per cent solution of acetic acid (for alkaline encrusted cystitis).

Uses of Tidal Drainage. Tidal drainage is applicable to numerous bladder conditions. (1) It is particularly useful in preventing the occurrence of infection in neurogenic vesical dysfunction. In these cases, tidal drainage diminishes the urinary sepsis attending the use of the indwelling catheter. If the bladder is not already infected, prolonged drainage can be accomplished without introducing infection if proper precautions are used.

(2) It is a valuable adjunct in the treatment of acute or chronic cystitis, particularly those cases with marked infection or encrustations that do not respond to oral therapy and other recognized measures.

(3) It may be used to increase the capacity of a contracted fibrotic bladder. This is accomplished by progressively increasing the height of the siphon-tube over a period of weeks.

(4) It may be used wherever an indwelling catheter or repeated catheterization is indicated "with the advantages that antiseptic solution is almost continuously in contact with the bladder walls, and that it will not allow the progressive contracture of the bladder which occurs with an indwelling catheter draining away continuously." (Lawrie and Natban)

W. G. Hayward stresses the superiority of tidal drainage of the bladder over both the ordinary catheter drainage and cystostomy for preliminary treatment of the surgical prostate, and urges that it be used more often for this purpose.

Chemotherapy

This section applies not only to diseases of the bladder, but to genito-urinary infections in general.

(1) The Sulfonamides in the Treatment of Urological Conditions

By far the most generally useful of the drugs at present available for the treatment of genito-urinary infections are the sulfonamides, the clinical employment of which goes back only to 1937. These are specific drugs which have a powerful effect on some bacteria and no effect on others. Unaffected organisms may have a natural or an acquired resistance.

In 1935, Domagk observed that azo compounds containing sulfonamide exerted a selective action on hemolytic streptococcal infections in mice. Soon he demonstrated their value in the treatment of such infections in man. Tréfouel, *et al.* (1935), after studying many similar compounds, suggested sulfanilamide, a colorless compound of equal effectiveness and less toxicity than those originally used. Colebrook and Kenny, Long and Bliss, Helmholz, Marshall, and others did much experimental work to prove the efficacy of sulfanilamide. Dees and Colston (1937) were the first in America to record their results with sulfanilamide in the treatment of gonorrhea.

During the past 8 years, research has resulted in the synthesis and study of a vast number of sulfanilamide derivatives and allied compounds. As a result of the attempt to find a derivative with a minimum of toxic action while retaining maximum effectiveness, numerous sulfonamide drugs have appeared on the market in rapid succession. At the

present time, five of these chemicals are successfully and widely utilized in the treatment of human diseases. All of these five—sulfanilamide, sulfapyridine, sulfathiazole, sulfadiazine, and sulfaguanidine—have received quite extensive clinical trial in urological practice, and will be considered below.

Mode of Action of Sulfonamides. The action of the sulfonamides is essentially bacteriostatic, and is believed to depend upon oxidation which inactivates certain enzymes and inhibits bacterial growth. Since the action is bacteriostatic, destruction of the bacteria must be completed by the natural defense mechanisms of the body. The antibacterial action of these drugs is greatly decreased when large numbers of organisms are present, as well as when there is tissue destruction with necrosis and purulent exudate.

Pharmacology of Sulfonamides. In general, all sulfonamides act alike, although the individual variations are great enough to make some much to be preferred over the others for special urological use. They all form the active and the inactive, or conjugated, forms in the blood and urine. Their pharmacological activity depends upon solubility, absorption, excretion, and acetylation.

The drugs are eliminated almost entirely through the urinary tract, the rate of renal excretion varying with the individual chemical. Sulfanilamide is excreted with moderate rapidity. With sulfapyridine the rate is variable. Sulfathiazole is excreted very rapidly, making it difficult to maintain an adequate blood level; while sulfadiazine is eliminated slowly, making it easy to maintain an adequate therapeutic blood level.

The sulfonamide compounds also differ considerably in their solubility. Sulfanilamide is relatively soluble, and renal complications are rare. Sulfapyridine, sulfathiazole, sulfadiazine, and their acetyl forms, on the other hand, are relatively insoluble, particularly in acid urine, and renal complications occur frequently.

The acetyl derivatives, which are therapeutically useless, appear in the blood and urine in approximately the same percentage for each drug irrespective of the route of administration. The amount of acetylation does not depend upon the concentration of the drug in the blood stream. The acetylated forms are ordinarily non-toxic in the amounts formed. However, hematuria, renal insufficiency, and even stone-formation may result from the deposition of crystals of the acetyl derivatives in the urinary tract.

Sulfanilamide. The oldest of the sulfonamide drugs—sulfanilamide—

has been largely superseded by newer compounds which are less toxic and more effective in most infections. Sulfanilamide is still the drug of choice, however, in hemolytic streptococcal and gas bacillus infections. It is also effective in gonorrhea, Dickey bacillus infection (chancroid), and infections caused by the *Bacillus coli* and the *Bacillus proteus*; these, however, are now treated largely by the newer and better tolerated compounds, such as sulfathiazole and sulfadiazine—sulfanilamide being used, as a rule, only if these are not effective.

Given orally, sulfanilamide is readily absorbed from both sections of the intestinal tract, so that adequate blood concentration soon occurs. Fully 90 per cent of the amount thus absorbed is excreted by the kidneys in a single day, the drug attaining a concentration in the urine 10 to 20 times greater than in the blood.

The recommended oral dosage for a serious infection in an adult weighing 60 kg. (130 pounds) is an initial dose of 5.4 Gm. followed by a maintenance dose of 0.9 Gm. every 4 hours, day and night. After the temperature has been normal for 24 hours, the dose may be cut in half. When the patient is moderately ill, the initial dose should be reduced to 4 Gm., but the maintenance dose should be the same as in severe infections. Small doses—1.8 to 2.7 Gm. daily—are used for ambulatory patients, for infections amenable to small amounts of sulfanilamide, for those who do not tolerate the drug well, and when the drug is to be administered over considerable periods of time. For children, one-half to three-quarters the adult dosage should be used; and for young infants, one-third, or never more than one-half, the adult dosage is sufficient.

The usual course of treatment is 10 to 14 days if the drug is well tolerated. Therapeutic response is usually evident within 48 hours. After clinical improvement, the dose is gradually decreased. If there is no clinical response in from 5 to 7 days, the drug should be stopped.

There is great risk of toxic effects with massive doses of sulfanilamide, and the blood sulfanilamide level, hemoglobin, and red and white cell count must be checked daily while they are being given. As a rule, the toxic manifestations are proportional to the amount of the drug ingested, although the tolerance of individual patients varies greatly. The condition of the kidneys, especially with respect to function, is to be considered before subtoxic doses of sulfanilamide are given. Seriously impaired renal function is contraindicated to the use of sulfanilamide in amounts greater than 1.8 Gm. daily.

Since sulfanilamide tends to produce an acidosis, sufficient bicarbonate of soda should be given to render the urine neutral or alkaline in reaction.

Sulfanilamide is usually given orally, but if it cannot be taken by mouth, it may be injected subcutaneously. Intravenous administration is not advisable or necessary.

Sulfapyridine. While sulfapyridine has proved effective in a number of infections, it has been most useful in pneumonia. Its chief urological use has been in the management of gonorrhea. This drug is excreted much more slowly by the kidneys than is sulfanilamide, and, in comparison with the latter, is less soluble and therefore not so readily absorbed from the intestinal tract. If administered orally, much of it will not be absorbed at all, and can be retrieved almost completely from the feces.

Helmholz, experimenting with 10 different strains of *Staphylococcus aureus* to determine the relative usefulness of sulfapyridine, sulfathiazole, sulfadiazine, and sulfacetimide in the control of infections of the upper urinary tract, found that "sulfapyridine does not exhibit nearly the bacteriostatic effect that the other three sulfonamide compounds do at any of the four concentrations" which he tried. He concluded: "Inasmuch as high figures for turbidity indicate a low degree of bacteriostatic power, the drug having the lowest average for turbidity has the greatest bacteriostatic action, and so, one gets a pretty good idea of the relative value of these compounds from the following averages of the degrees of turbidity: sulfathiazole, 0.57; sulfacetimide, 1.47; sulfadiazine, 1.74, and sulfapyridine, 3.03." These findings of Helmholz confirm the general testimony of writers on urological subjects, most of whom have found that sulfapyridine is not of outstanding value except in the treatment of gonorrhea.

In the management of gonorrhea, relatively small doses of sulfapyridine—2 Gm. daily in 4 doses—have proved effective in a high percentage of cases.

When sulfapyridine is administered orally, certain patients do not attain a sufficiently high blood concentration of the drug to make the therapy effective. For them, the monohydrate sodium salt—sodium sulfapyridine—intravenously injected, is preferable, at least for the initial dose. Intravenous administration is also useful when oral therapy is, for any reason, impossible, or when enough of the drug cannot be absorbed from the alimentary tract (for example, in persistent vomiting) to control the infection. It is customarily given in a 5 per cent solution, either distilled water or physiological saline being the medium. To obtain a blood level of 5 to 8 mg. per cent, a dosage of 0.03 Gm. per pound of

body weight is the standard, with a maintenance dosage of 0.015 Gm. per pound of body weight.

Sulfapyridine is relatively well tolerated by the majority of patients. Serious toxic reactions occur less frequently than with sulfanilamide, but minor toxic reactions (fever, drug rash) are common.

Kalak water has been found useful in counteracting two distinct disadvantages of sulfapyridine: (1) the occurrence of nausea and vomiting, and (2) the tendency to the formation of calculi composed of acetylated sulfapyridine. If enough water is given to cause methyl-red paper to become distinctly yellow when dipped in urine, the crystals of the acetylated form of the drug will be dissolved, and the loosely combined aggregate of crystals, designated as "calculi," will disintegrate, thus obviating the trauma to the renal pelvis and tubules responsible for hematuria. In counteracting vomiting, Kalak water serves well as a vehicle for administration, when the drug is taken orally. Fifty cc. of the water may be used for disintegrating and suspending the drug, with a total intake thereafter up to 1,500 cc. each day.

Sulfathiazole. Sulfathiazole, evolved by Fosbinder and Waters in 1939, is extensively used in urological practice. Not only is it more rapidly and uniformly absorbed than sulfanilamide and sulfapyridine, but there is less conjugation after absorption and less tendency to cause serious nausea and vomiting. It is quickly excreted in the urine, from 80 to 90 per cent being eliminated in 24 hours.

At the Brady Foundation, of the New York Hospital, sulfathiazole is given orally, intravenously, and as a powder for dressing open wounds, and has proved satisfactory in all three requirements. It is especially useful in all types of gonorrheal infection, but particularly urethritis in the male—all signs of the infection frequently disappearing in from 48 to 72 hours. In addition, it is the most effective drug (except penicillin) against the *Staphylococcus aureus*, and is very useful in the treatment of genito-urinary infections due to the *Bacillus coli* (*Escherichia*), *Bacillus pyocyaneus*, *Streptococcus faecalis*, and *Aerobacter aerogenes*.

In both acute and chronic gonorrheal infections, sulfathiazole has produced a high percentage of cures, in less time than sulfanilamide and sulfapyridine and with fewer and milder side-effects. Blood levels of 1.5 to 3 mg. per cent are effective. Adult patients are usually given 2 Gm. daily, in 4 doses, for from 7 to 10 days. The initial response is usually rapid. In chronic infections, it may be necessary to give a second course of medication, of similar amount and duration, after a brief rest period.

In urinary-tract infections, the usual dosage is 2 Gm. followed by 1 Gm. every 6 hours, producing a blood level of 3.0 to 3.5 mg. per cent.

The recommended dosage for infants and children is 30 mg. per pound of body weight.

Sulfathiazole, in conservative doses (2 Gm. daily), is particularly useful before and after urological operations, to prevent or combat infection. Non-specific infections of the bladder following transurethral resection of the prostate gland have proved especially amenable to small doses of this drug. The infection is not eradicated within two or three days, but the relief from dysuria, frequency, etc. is, often very marked.

Sodium sulfathiazole can be given intravenously—with Ringer's solution, dextrose, or distilled water as the medium. It is available in 10 cc. ampoules of 25 per cent concentration (2.5 Gm.).

Severe toxic reactions are infrequent with sulfathiazole, and it produces less nausea and vomiting than sulfapyridine. It is claimed that skin rashes and conjunctivitis are more often encountered with sulfathiazole than with the other sulfa drugs, but this has not been our experience. The tendency to crystal formation in the urine is about the same as with sulfapyridine, and greater than with sulfanilamide; this can be overcome by giving plenty of fluids and keeping the urine alkaline by the administration of sodium bicarbonate (see p. 1172). It is generally conceded that individuals with kidney impairment excrete sulfathiazole very poorly, as the damaged kidney is unable to concentrate the drug.

Sulfadiazine. Sulfadiazine has been found to be effective in most of the urological conditions benefited by sulfonamide therapy. It is readily absorbed into the blood stream, and is not excreted as rapidly as sulfathiazole, disappearing slowly from the blood. Small quantities of sulfadiazine will maintain a high level in the blood. It readily diffuses into the pleural and ascitic fluids, and at a somewhat slower rate into the cerebro-spinal fluid. It is definitely the least toxic of the sulfonamides, and appears to have less tendency to form crystals in the urine than sulfathiazole. At the Brady Foundation, we have found it satisfactory for both oral and intravenous administration, as well as for use, in powder form, in open wounds. This drug is of proved merit in both acute and chronic gonorrheal infections and in most of the more common non-specific infections occurring in the urinary tract. Because of its antibacterial action against many types of bacteria and the absence of toxic side-effects, it is widely used by urologists.

In both gonorrheal infections and non-specific urinary-tract infections,

3 Gm. of sulfadiazine daily, in 4 doses, is usually satisfactory. In a large series, representing all types of urinary-tract infections, L. F. Greene and his co-workers gave sulfadiazine regularly—3 Gm. daily, in divided doses. In some cases as little as 1.5 or 2 Gm. daily sterilized the urine, though in others considerably higher dosage was required. There were fewer unpleasant side-effects than had been encountered previously, when other sulfonamides had been given.

From 2 to 3 Gm. of sulfadiazine daily, in divided doses, before and after urological operations, has been found very useful in preventing or combating urinary infection, and in reducing to a minimum the incidence of postoperative pneumonia and wound infections.

For children, the recommended dosage is as follows: 6 months and under, 0.5 Gm. followed by 0.25 Gm. 4 times daily; 6 months to 3 years, 1 Gm. followed by 0.5 Gm. 4 times daily; 3 to 10 years, 2 Gm. followed by 0.5 Gm. 4 times daily.

If an adequate blood concentration cannot be obtained by oral administration alone, oral treatment may be supplemented by the intravenous injection of sodium sulfadiazine. Intravenous administration is also indicated in patients who are unable to take the drug by mouth, and in critically ill patients who require immediate and adequate medication to save life. Sodium sulfadiazine is available in 10 cc. ampoules of 25 per cent concentration in distilled water (2.5 Gm.). The injections should be made slowly, care being taken to prevent the solution from entering the subcutaneous tissues. The dosage of 2.5 Gm. may be repeated in 6 to 12 hours, depending upon the concentration desired, and whether the drug is being given intravenously only or also by mouth.

Although hematuria and urinary crystallization are less frequent with sulfadiazine than with sulfathiazole and sulfapyridine, their occurrence is relatively common. It is, therefore, important that the patient take plenty of fluids and that his urine be kept alkaline by the administration of sodium bicarbonate in sufficient amounts (p. 1172).

Paradoxically, in the lack of toxic side-effects lies one of the chief dangers of sulfadiazine therapy. The absence of gastrointestinal disturbances permits patients to take this drug over a longer period of time and in larger doses than is usual with the other sulfa drugs. Overconfidence on the part of the physician, due to the lack of toxic manifestations, may permit renal complications to develop insidiously. These vary from transitory hematuria to anuria and death. The strict observation of the patient and frequent examination of the blood and urine

that are necessary with other sulfatherapy are just as important when sulfadiazine is being given, despite the greater tolerability of most patients to this drug.

Sulfaguanidine. Sulfaguanidine has a more limited usefulness than the other sulfa drugs, being employed chiefly in bacillary dysentery and preoperatively in intestinal surgery. Because it is poorly absorbed from the digestive tract, and produces low concentrations in the blood and tissues, it cannot be used as a substitute for sulfanilamide or other sulfa compounds. It has, however, a high bacteriostatic action against many of the bacteria which may occur in the gastrointestinal tract.

In urological practice, sulfaguanidine has proved a valuable aid in the prevention of infection of the upper urinary tract following transplantation of the ureters to the sigmoid. The drug is given orally for 4 or 5 days before operation, the recommended dosage being 0.05 Gm. per kg. of body weight every 8 hours, day and night. As soon as possible after operation, the same dose of the drug is started again by mouth and continued for from 5 to 7 days.

Use of Sulfonamides in Surgical Wounds. In operations upon infected kidneys, or in extensive traumatic injuries involving parts of the urinary tract, sulfonamides introduced directly into the operative wound are proving increasingly useful. In a series of experiments carried out by Walter and Cole, the effect of crystals of both sulfanilamide and sulfadiazine placed in the peritoneal cavity was studied both with animals and human patients. They found that sulfadiazine was regularly superior to sulfanilamide, being not only less toxic but having a far wider range of specificity, as it is effective against the hemolytic streptococcus and many other bacteria. They found a much more persistent blood level with sulfadiazine than with the older compound. Sulfonamide drugs were used in the peritoneal cavity following operation only in those cases where there was proof or reason to believe that contamination had taken place. When sulfadiazine is used, it should be spread evenly over the surface of the exposed area so that it will not accumulate in clumps, as these may cause a foreign-body tissue reaction which would delay healing. Six gm. was adopted as a routine dose, 4 Gm. being implanted in the peritoneal cavity and 2 Gm. in the wound at the end of the operation, the powder being evenly sprinkled over the entire surface.

At the Brady Foundation, we have for some time been placing from 1 to 3 Gm. of sterile sulfathiazole or sulfadiazine powder in grossly or potentially infected operative wounds, with very beneficial results. Too large

doses should be avoided, as there is always the danger of lowering the vitality of the tissues and thereby producing more harm than good.

Elsewhere in these pages we have mentioned several other local uses of the sulfonamides, such as in surgically drained abscess cavities, in the treatment of chancroidal ulcers, etc.

Complications of the Sulfonamides. The unfolding of the therapeutic possibilities of the sulfonamides has brought with it increasing recognition of the unpleasant and occasionally serious side-effects which may attend their administration. These are exceedingly potent chemicals, and no satisfactory explanation of their mechanism of action has yet been found. Even in the case of the newer derivatives of relatively low toxicity, the potential harmful effects, and the varied response of individuals, must always be considered.

The toxic manifestations are usually transitory and mild in form, and include headache, anorexia, nausea, dyspnea, slight cyanosis, slight acidosis, and drug rash. As a rule, these subside promptly on decrease of the dose or, if the symptoms are more pronounced, withdrawal of the drug and forcing of fluids.

Besides these reactions, which are common to most drug idiosyncrasies, more serious toxic manifestations may follow the use of the sulfonamides: drug fever, persistent and severe nausea and vomiting, severe acidosis, psychoses and delirium, toxic hepatitis, polyneuritis, and blood dyscrasias. Any of these chemicals is capable of inflicting severe injury on the blood, although these reactions are rare with sulfadiazine and relatively uncommon with sulfathiazole. Anemia, which may progress to the acute hemolytic type, leukopenia, methemoglobinemia, and agranulocytosis have all been reported. Leukopenia and agranulocytosis are more apt to occur in patients who have had large doses of the sulfonamides over a long period of time. Mild cyanosis alone is not usually regarded as an indication for discontinuance of the drug. However, with cyanosis the blood picture must be carefully watched for impending blood disorder, especially acute hemolytic anemia and agranulocytosis. Methemoglobinemia and sulphemoglobinemia also are frequently ushered in with cyanosis. The appearance of any blood dyscrasia indicates immediate cessation of the drug and appropriate constitutional treatment: forcing of fluids, alkalinization, iron and liver tonics, and blood transfusions as indicated.

Drug fever is rare with sulfadiazine, but occasionally occurs with sulfathiazole and quite frequently with the older compounds. These patients

usually become cyanotic and their nails turn blue. Drug fever may be suspected if a patient suddenly develops fever, chills, headache, and malaise after there has been a marked improvement in his general physical condition. Immediate withdrawal of the drug is indicated. The forcing of fluids and administration of methylene blue pills will hasten recovery. The differential diagnosis between the development of a new focus of infection and drug fever must be made with care, but in doubtful cases it is better to play safe and stop the drug. If the temperature is due to the drug, it will subside to normal or be markedly reduced within 24 hours.

If liver function is known to be poor, or the patient gives a history of previous "liver trouble," the use of a compound which experience has shown causes hepatic disturbance is contraindicated. As sulfanilamide has been proved to have this effect, it should be avoided and sulfapyridine or, preferably, sulfathiazole or sulfadiazine used instead.

Renal complications, varying from slight hematuria to anuria, calculus-formation, nitrogen retention, uremia, and death, are, unfortunately, quite common, even with the relatively non-toxic sulfadiazine, as many recent reports in the literature bear witness. Newman and Shlessor have reported the removal of a sulfonamide renal calculus *two years* after sulfapyridine therapy. These complications are considered below.

Only recently has it been shown, both by postmortem and clinical evidence, that definite myocarditis may occur as a direct result of these drugs in patients who, previously, presented no evidence of organic heart disease.

Renal Obstruction Due to Crystalline Deposits. Renal obstruction during treatment with sulfapyridine, sulfathiazole, and sulfadiazine has been frequently reported in the recent literature, and is attributed to the poor solubility of these drugs and their acetyl derivatives. Sulfanilamide, being a relatively soluble drug, is less apt to cause renal complications.

So-called "sulfonamide anuria" may be (1) mechanical, and due to blockage of the ureters or uriniferous tubules by crystalline deposits, or (2) chemical, and due to acute toxic degenerative nephritis caused by calcifying necrosis. In the latter type, the convoluted tubules of the kidney are filled with small, brown particles of gravel-like material, tissue damage being associated with the toxic effect of the crystals of the acetyl drug rather than with reactive phenomena such as secondary infection (Mathé). Because of the tendency toward intratubular precipitation of

crystals of sulfathiazole and sulfadiazine, renal complications may be more serious than those found with sulfapyridine.

Crystallization is now known to occur more readily in acid urine; therefore, maintenance of a consistently alkaline urine by the administration of sufficient alkalis is regarded as the surest means of preventing renal complications during sulfathiazole and sulfadiazine therapy.

The investigations of Fox, Jensen, and Mudge showed that there is a very sudden and decided increase in the solubility of sulfathiazole, sulfadiazine, and their acetyl forms as the urine is made alkaline, which they explained on the basis that these drugs and their acetyl derivatives are weak acids which ionize and form soluble salts in an alkaline urine. They state:

As the pH is raised from 5.0 to 7.0 there is little salt formation and the solubility in urine is not appreciably decreased; from pH 7.0 to 8.0, however, there is extensive salt formation and the solubility of sulfathiazole and sulfadiazine, both free and acetyl, is greatly increased. In the case of sulfapyridine and its acetyl form, on the other hand, extensive salt formation does not occur until pH 9.0 and 10.0 respectively are reached—beyond the pH range of urine; this accounts for the failure of alkali therapy to prevent renal precipitation of this drug. With sulfanilamide, salt formation does not occur until pH 10.6 is reached; but, in contrast to the preceding drugs, it is a relatively soluble substance.

They further state:

It is important to realize as these drugs are secreted by the kidney a concentration of 10 mg. per 100 cc. in the blood may be increased to 300 mg. per 100 cc. in the urine as a result of reabsorption of water by the tubules. In addition, base is also reabsorbed and the pH may be lowered from that of the blood (7.4) to as low as 5.5, commonly found in the urine. By thus lowering the pH in the case of sulfathiazole, sulfadiazine and their acetyl forms, the soluble salts are converted to the relatively insoluble acids, and precipitation takes place. The function of the alkali is to prevent this fall in pH during the formation of urine.

These investigators believe that the quantity of alkali needed to prevent obstructive crystalluria should be governed primarily by the pH of the urine (which should be measured frequently) and not by the amount of sulfonamide given. "To maintain sulfadiazine in solution during full therapeutic dosage, a pH of 7.5 or more is essential."

Gilligan and his associates at Cornell University Medical College studied the solubilities of sulfadiazine and its conjugation products, and found that at a pH of 5.2 there was an acetylsulfadiazine solubility of about 10 mg. per 100 cc., which was increased to 60 mg. at pH 6.5. With

alkaline urine (pH 7.5) the solubility was over 500 mg. per 100 cc., which is a solubility from 10 to 50 times greater than in acid solutions. Clinically, it was noted that in 172 patients, whose urine was acid, crystals appeared when they were put on sulfadiazine therapy; but 147 patients, whose urine was rendered alkaline by the oral administration of sodium bicarbonate before sulfadiazine therapy was begun, yielded but two specimens showing crystalluria, and these cleared up when further sodium bicarbonate was given. These workers used from 13.7 to 19.5 gm. of alkali daily in 6 doses, and found it well tolerated in all instances. They warn, however, that these figures are high in patients suffering renal or cardiac insufficiency.

There seems to be general agreement among those who have carefully studied the subject that the prevention of crystal deposition is best accomplished by reducing the dosage of the drug to a maximum of 4 gm. daily, maintaining the blood level below 8 mg. per 100 cc., forcing fluids to a daily urine output of 1,200 to 1,500 cc., and alkalinizing the urine to a sustained pH of 7.5 by the administration of sodium bicarbonate.

Crystalluria is not in itself adequate reason for discontinuing sulfatherapy. In most cases, the crystals pass through the urinary tract with no injurious effects. Not infrequently, however, they accumulate in the renal tubules, papillae, or pelves, or in the ureters, obstructing the outflow of urine. Factors that undoubtedly favor the accumulation of crystalline deposits, in addition to acid urine, are obstructive lesions of the upper and lower urinary tracts, stasis, infection, and prolonged use of the sulfonamide. Mathé points out that, with sulfadiazine, renal complications are much more likely to occur during a second course of therapy.

Signs and symptoms pointing to renal obstruction and impending anuria are: dull, aching pain over the lumbar and suprapubic regions, colic (occasionally), kidney tenderness, azotemia, reduction in the amount of urine, and finding in it crystals, red blood cells, and albumin. Frequently there is nausea and vomiting.

The occurrence of these symptoms is indication for immediate withdrawal of the drug and the administration of alkalis, forcing of fluids, and intravenous injection of glucose. In some cases this may result in the resumption of urinary excretion. If anuria persists, ureteral catheters should be passed to the renal pelves, or as far up the obstructed ureters as possible, and the pelves and ureters lavaged with warm sodium bicarbonate solution, as advocated by Fox and his associates. This solution dissolves the drug crystals much better than warm water or isotonic

solution of sodium chloride, in which these drugs are very slightly soluble. In fact, these authors believe that the utilization of renal pelvic lavage with sodium bicarbonate solution "in routine therapy with sulfathiazole and sulfadiazine in average doses would remove the hazard of their renal complications." The mere passage of the catheters often dislodges showers of crystals in the ureters. Retention catheters should be left in place for 24 hours or as long as necessary to drain and irrigate away most of the crystals. If it is impossible to pass catheters up the obstructed ureters, or at least to one renal pelvis, nephrostomy drainage must be carried out at once. Time is an extremely important factor in these cases.

General Rules for Sulfonamide Therapy. It cannot be too often emphasized that any patient taking a sulfonamide compound should be carefully watched throughout the course. Whenever possible, the patient should be under hospital supervision. If he must of necessity be ambulatory, he should have daily medical supervision for evidence of toxicity or renal obstruction, and his conduct should be strictly regulated. Ambulatory patients should be warned of possible dangers and urged to report promptly the slightest indication of untoward reactions. They must refrain from all alcoholic drinks, and under no circumstances drive motor vehicles, as disorientation is common even without serious reaction.

Not until we have had greater experience with these valuable but potentially dangerous drugs can any set rules for the avoidance of complications be laid down. Certain general principles should, however, be observed:

1. *Restriction of Dosage.* Two Gm. of a sulfonamide drug daily, in divided doses, is the maximum safe dosage for ambulatory patients. For hospitalized patients and those under constant competent supervision, larger doses are permissible, and are often advisable. However, it is our belief that many of the serious complications that have occurred with sulfonamide therapy undoubtedly have resulted from overdosage, particularly in the beginning of its administration. In common with many urologists, we have not found large doses of the sulfonamides necessary in urological practice, and customarily give smaller doses than the average practitioner.

2. *Adequate Intake of Fluids.* An adequate intake of fluids (2,500 to 3,000 cc. daily) is very important when any sulfonamide is being taken, but particularly in therapy with sulfapyridine since, with this drug, alkalization of the urine is less effective in preventing precipitation of crystals than with sulfathiazole and sulfadiazine.

3. *Alkalinization of the Urine.* Alkalinization, with the pH of the urine as a guide, is of particular importance in sulfathiazole and sulfadiazine therapy. This has been considered in the foregoing section on renal obstruction. It is our practice to give at least 2 gm. of sodium bicarbonate with each dose of a sulfonamide drug, which usually is satisfactory with the moderate dosage employed by us. Larger doses of alkali may, however, be necessary.

4. *Frequent Examination of Blood and Urine.* It is especially important to watch for a reduction in the hemoglobin, as this may lead to increased leukocyte production, demonstrated on blood examination by the presence of many immature cells. Regular blood examination throughout the course of sulfatherapy should include hemoglobin estimation, red blood corpuscle and leukocyte count, and differential count of the white cells. If anemia develops rapidly, or immature leukocytes develop in the blood stream, the drug must be at once withdrawn. Very severe reactions may require blood transfusion.

Because of the likelihood of crystal formation, the urine should be carefully watched and any indication of hematuria promptly noted. Retention and oliguria are other danger signals requiring prompt action.

5. *Withdrawal of the Drug on Appearance of Certain Reactions.* Withdrawal of the drug is indicated if drug fever, drug rash, severe nausea and vomiting, infection of the sclera or conjunctiva, or cyanosis is noted. Usually the prompt discontinuance of the drug will cause these unfavorable side-effects to disappear.

It is obvious from the above that, while the sulfonamides have a wide field of usefulness, being very effective in many diseases, their administration is not without danger. Their use in the right instances, with careful control, has achieved notable successes in treating infections; but they should not be used in infections that are so mild that the danger of the toxic reactions offsets the danger of the disease.

Method of Determining Concentration of a Sulfonamide Drug in Blood and Other Tissue Fluids. The method described here is applicable for determining the concentration of the known sulfonamides in the body fluids of man or animals. This method was developed in the laboratories of Dr. E. K. Marshall, Jr., of Johns Hopkins University.

The reagents necessary for this determination are as follows:

1. A 15 per cent solution of trichloroacetic acid in distilled water.
2. A 0.05 per cent solution of saponin in distilled water.
3. A 0.1 per cent solution of sodium nitrate (very pure grade and to be prepared fresh each day).

4. A 0.1 per cent solution of N-(1-naphthyl)-ethylene diamine dihydrochloride (to be kept in a dark-colored bottle).
5. A 4N solution of hydrochloric acid.
6. A 0.5 per cent solution of ammonium sulfamate in distilled water.
7. A solution of the compound under test, i.e., sulfanilamide, sulfapyridine, sulfathiazole, etc., containing 10 mg. per 100 cc. of distilled water. This solution serves as the stock solution, and may be kept for long periods in the dark and in the refrigerator.

To prepare working standards from the stock solution, a sufficient quantity of the stock is diluted with 18 cc. of trichloroacetic acid, then brought to 100 cc. volume with distilled water so that the final working standards contain 0.2, 0.5 and 1.0 mg. per cent, respectively. Tissue fluids will usually fall within the range of one of these standards. The stock standard may be made up to 20 mg. per cent, but some of these compounds will go into solution at that concentration with difficulty. It is therefore advisable to use 10 mg. per cent.

Procedure for Blood. Two cc. of oxalated blood is measured into 30 cc. of the saponin solution with shaking, and, after a few minutes, to allow for the laking of the blood cells, 8 cc. of the solution of trichloroacetic acid is added to precipitate the blood proteins. After a few minutes the precipitate is filtered off, and the compound under test is determined in the filtrate by adding 1 cc. of the sodium nitrate solution to 10 cc. of accurately measured filtrate. After 3 minutes' standing, to allow for diazotization, 1 cc. of the sulfamate solution is added. Two minutes are allowed and then 1 cc. of the N-(1-naphthyl)-ethylene diamine dihydrochloride is added. Within 5 minutes the color that is formed will be complete and the comparison may be made in a colorimeter with an appropriate standard, 10 cc. of which has been treated in the same manner as the 10 cc. of filtrate. The amount of compound under test in the unknown tissue fluid is then computed from the reading in the colorimeter.

The use of the following representative formula is helpful:

$$\frac{S \times C \times D}{R} = \text{mg. per 100 cc.}$$

S = concentration of the standard employed, i.e., either 0.2, 0.5 or 1 mg. per cent.

C = the setting at which the standard solution was put on the colorimeter.

D = the dilution to which the unknown sample was subjected.

R = the reading on the colorimeter on the unknown side.

All determinations should be made at a uniform temperature.

(2) *Other Urinary Antiseptics*

Methenamine. One of the most useful drugs for the treatment of colon bacillus and staphylococcus infections of the urinary tract, and one that has been widely employed for more than a quarter of a century, is methenamine (hexamethylenamine), which was introduced as a urinary antiseptic in 1894 by Nicolaier, who called it *urotropine*. It is chemically stable, non-toxic, and inexpensive, and can be administered in large quantities without injury. It is excreted unchanged by the kidneys, and becomes active in the urine through the formation of formaldehyde. While methenamine is not in itself bactericidal, the formaldehyde which it liberates is an efficient germicide. The splitting of methenamine into formaldehyde and ammonia takes place only in acid urine. A pH of below 5.6 is necessary if a sufficient amount of formaldehyde is to be generated. Helmholz showed that a dose of methenamine at a pH of 5.0 gave cultural death in 24 hours, whereas ten times the original dose at a pH of 6.0 gave no bacteriostasis.

In making use of methenamine it is important to bear in mind that its action depends not only upon the acidity of the urine but also upon the reaction time of the conversion of its elements into formaldehyde (Hinman). The acidity of the urine is influenced by both metabolic and bacterial changes. In the absence of bacteria, the reaction is usually acid. When the urine is neutral or alkaline from either disease or diet, the utilization of a high acid ash diet and the oral administration of acidifying drugs, such as acid sodium phosphate, sodium benzoate, and ammonium chloride or nitrate, will quickly render it acid. The alkalinity of the urine, due to the presence of organisms which decompose the urea, cannot as a rule be changed by the administration of acid-producing drugs. The value of methenamine for bladder conditions in which there is frequency, or where continuous drainage has been established, is largely destroyed by the necessity for time to permit accumulation of formaldehyde in antiseptic amount.

Methenamine is particularly useful in cases where medication must be given over long periods of time, as in cord bladder with residual urine. The drug has the advantage of being effective regardless of the kidney function. In office practice, many patients can tolerate methenamine and remain ambulatory, whereas with mandelic acid or the sulfonamides they are unable to do so.

For the treatment to be effective, the methenamine and acid sodium phosphate, or other acidifier, must be given in sufficiently large doses—

not less than 4 Gm. a day, in 3 or 4 doses. A high acid ash diet may be used in combination with the drug therapy.

Mandelamine. A newer drug of the same class as methenamine—methenamine mandelate, marketed under the trade name *mandelamine*—has given excellent results in the service of Kirwin, and seems to offer marked advantages over the older compounds. It has been used extensively in simple cystitis and the bladder inflammation induced by prostatic hypertrophy; but it is in renal infections, particularly, that its efficiency has been notable. The average dose is 3 tablets 3 times daily, each tablet containing 0.25 Gm. of methenamine mandelate, making the total daily dosage 2.25 Gm.; of this, 1.18 Gm. is mandelate acid, and 1.07 Gm. methenamine, by analysis. The evidences of intoxication so often seen when using other forms of mandelic acid—nausea, vomiting, and gastrointestinal distress—have never, in our experience, been observed. The urine will often be cleared of organisms in from 3 to 5 days, though in certain cases it has been necessary to persist with the treatment for a longer period. The patient can remain on his regular diet throughout the course of treatment.

Hexylresorcinol. Hexylresorcinol (caprokol) for a time had a widespread popularity as a urinary antiseptic, but is now little used for this purpose. Coccal infections yield better to this drug than those due to the colon bacillus. It has the advantage of acting in both acid and alkaline urines.

Acriflavine. Acriflavine has definite usefulness, particularly in acute infections, but in a considerable proportion of cases it causes unpleasant gastrointestinal symptoms, thus limiting its clinical value as an internal antiseptic. In an alkaline urine it exerts a bactericidal effect against both the staphylococcus and colon bacillus. Its antiseptic action is fairly rapid, appearing 2 hours after administration and lasting at least 8 hours.

Methylene Blue. Methylene blue, the best known of the group of diphenylamine dyes, has proved anti-staphylococcal properties, but it has an irritative effect on the digestive system, and with decreased renal function, there may be marked renal irritation. We frequently use this drug in cases of urogenital tuberculosis, where it is often very useful in relieving the distressing vesical symptoms. Other urologists use it regularly for patients who have had transurethral resections. It appears to have but little bactericidal effect on the common bacillary infections. The usual dosage is 0.06 Gm. 4 times a day. It has been found that the

staphylococcus quickly adapts itself to the dye and becomes immune to its effects after a relatively short time; therefore, temporary discontinuance of the drug is advisable.

Pyridium and Other Azo Dyes. Pyridium, serenium, niazo (neotropin), and other azo dyes have entered the field of urinary antiseptics relatively recently. As with most urinary antiseptics, opinions differ widely regarding their efficacy. Their low toxicity and the fact that they act in both alkaline and acid urines have won them numerous adherents, particularly in the treatment of infections produced by the gonococcus and staphylococcus. On the whole, however, their bactericidal properties have been found to be very slight.

For stubbornly alkaline urine, pyridium, 0.1 Gm. 3 times a day has been found useful.

Oil of Santal. Oil of santal has been widely used for centuries as a specific for gonococcal urethritis. Although much less popular than formerly, it is still regarded as a useful drug in the treatment of gonorrhea.

Neoarsphenamine. This antiseptic is used specifically for resistant coccal infections. Pace found that neoarsphenamine, as a source of urine arsenic, is bacteriostatic and probably bactericidal in a concentration of nine parts per million. It is used in infections due to *Staphylococcus aureus*, *Micrococcus catarrhalis*, and *Streptococcus faecalis*. The chemical nature of the excreted arsenic is unknown.

The usual dosage is 0.2 Gm. given intravenously, followed by 0.3 Gm. in 5 to 7 days. When no improvement follows two or three such doses, larger or additional doses are rarely effective.

Mandelic Acid. After several years of clinical trial and evaluation, mandelic acid has proved its bactericidal potency in the treatment of certain urinary infections, and has gained widespread acceptance as a relatively simple and rapidly effective method of combating certain of the organisms commonly found in the urinary tract, notably the colon bacillus.

Mandelic acid was introduced as a urinary antiseptic by Rosenheim in 1935 as the culmination of a search for a therapeutic agent that might replace the cumbersome and unpleasant ketogenic diet in the treatment of urinary infections. In 1933 Fuller showed that β -hydroxy-butyric acid—one of the keto-acids—is the active bacteriostatic agent in the urine of patients being treated for urinary infections with the ketogenic diet. Oral administration of β -hydroxy-butyric acid itself, however, proved ineffective because it is completely oxidized before it is excreted by the kidneys. A search was then begun for a keto or hydroxy-acid

which would combine effective bacteriostatic power with resistance to oxidation. Such an acid, if non-toxic and if excreted unchanged in the urine, should be able to replace the ketogenic diet. In 1935, after rejecting several other agents, Rosenheim introduced as a urinary anti-septic mandelic acid, an aromatic hydroxy-acid (known chemically as a hydroxyphenylacetic acid) which, as early as 1883, had been shown by Schotten to be excreted unaltered in the urine of dogs.

Mandelic acid escapes metabolism in the animal organism and, when orally administered, is excreted in the urine in a concentration of from 0.25 to 1 per cent, which, at a pH ranging from 5.0 to 5.7, is sufficient to kill most of the agents of the more common urinary infections. The more acid the urine, the more pronounced the bactericidal effect of the mandelic acid and the less the concentration of the acid required.

The urinary pathogen that has responded best to mandelic acid therapy is the *Escherichia coli*. Series of cases have been reported by a long list of authors indicating that in uncomplicated bacillary infections sterilization of the urine may be expected in over 80 per cent of the cases. Other organisms which have responded to treatment, but less effectively, are *B. pyocyaneus*, *Aerobacter aerogenes*, *B. proteus*, staphylococci, and streptococci. *Streptococcus faecalis*, it has recently been found (Cook; Helmholtz), can usually be eradicated by this drug. The elimination of the proteus organism from the urinary tract is difficult because of the frequent inability to maintain a sufficiently low pH of the urine.

Twelve gm. of mandelic acid daily, in 4 divided doses, given in the form of a salt, such as sodium or ammonium mandelate, is the method of administration recommended by Rosenheim and still followed by many advocates of mandelic acid therapy. It is best given after meals and at bedtime. Because of the gastrointestinal disturbances which frequently accompany the use of the drug, it may be necessary to start with a reduced dosage. The fluid intake is restricted to not more than 6 glasses of water (1,200 cc.), which should be properly rationed through the 24 hours in order that the urinary concentration of mandelic acid may be maintained as nearly constant as possible.

The urine must be kept at or below a pH of 5.6 to obtain the full therapeutic response.

In liquid form the drug is usually given as an elixir or syrup. In either form it is very disagreeable and often produces gastrointestinal upsets. Administration in the liquid form must be accompanied by a suitable acidifying agent (ammonium chloride, acid sodium phosphate, or am-

monium nitrate, 4 Gm.), to give the desired urine pH. Mandelic acid may be given in powder form as either calcium mandelate or sodium mandelate. The required dosage remains the same. Administration of the drug in pill form seems to be accompanied by far fewer gastrointestinal disturbances. Also, additional acidification is usually unnecessary.

Mandelic acid therapy, while easily administered, requires close observation of the patient and the urine. The acidity of the urine may be easily and satisfactorily tested by nitrazine paper and the nitrazine colorimeter, and should be determined daily for the first few days and at close intervals thereafter.

In the treatment of urinary infections, mandelic acid is usually given for one week after the urine becomes sterile, but should never be given for longer than 3 weeks. After several weeks of rest, the course may be repeated if necessary.

Most uncomplicated cases of urinary infection clear up fairly rapidly under proper treatment. If, therefore, the urine remains infected despite active treatment, search should be made for a persistent underlying cause of stasis, which would tend to keep the urine infected. Infections complicated by stone, prostatic hypertrophy, bladder diverticulum, stricture, etc., require more than the oral administration of mandelic acid or other urinary antiseptics to effect a lasting cure. The importance of urological study in persistent or recurring cystitis or pyelonephritis has been emphasized elsewhere. Mandelic acid has frequently proved successful in postoperative cases in clearing up the infection after the organic lesion has been treated surgically. It is also often used preoperatively in the hope of controlling the infection.

Transient nausea, vomiting, and diarrhea are the most common complications following the administration of mandelic acid. Tinnitus, headache, and urticaria have been reported in a few instances. No evidence of permanent impairment of renal function from its use has been observed, although slight temporary impairment has been noted by various observers. The drug should not be given over an indefinite period of time, however, and it should be administered with caution in patients with marked renal or liver impairment.

(3) *Penicillin*

Penicillin, the newest drug, is undoubtedly the most potent bacteri-killer so far to be discovered—much more potent than any of the chemicals of the sulfa family. Its greatest usefulness to date has been against

the staphylococcus, pneumococcus, gonococcus, and *Streptococcus hemolyticus*, and experimentation thus far has been confined largely to the treatment of infections produced by these organisms.

Historical Review. Penicillin was first discovered—quite by chance—by Dr. Alexander Fleming, of the University of London. While examining an agar plate on which he was growing disease-producing bacteria, his trained eye observed a fleck of green mold on the plate, and around the fleck was a ring of clear fluid. Some substance in the mold was destroying the bacteria. Fleming prepared crude extracts of penicillin, but because of the minute amounts available it was used only for laboratory purposes.

The mold in question was *Penicillium notatum*, a relative of the green mold in bread and Roquefort cheese.

In 1939, Dr. Howard Florey and his collaborators, of Oxford University, set to work to prepare pure extracts of the substance, and by a slow process of discarding chemical components of the mold that had no antibacterial effect, extracted a minute amount of yellow-brown powdery substance. After a series of experiments on mice, the substance was tried on human beings, with amazing results.

In 1941, Florey visited this country and enlisted the help of the National Research Council and the U. S. Department of Agriculture. In the Department's laboratory at Peoria, Illinois, studies were at once initiated on the characteristics of *Penicillium notatum* and on the methods of purification of penicillin. A few months later, four large pharmaceutical houses began growing the mold and extracting the drug. The supply was so small, however, that it was necessary to allocate it to the armed services for grave sulfonamide-resistant battle-wound infections, and to certain civilian hospitals for essential tests. Facilities for production and experimentation have been greatly expanded in recent months, spurred on by the urgent need for the drug in military medicine. Although much larger supplies are now available, they are still insufficient even for the armed services, and it is doubtful that the drug will be available to the general public for a long time to come.

The difficulties confronting large-scale production of penicillin arise chiefly from the fact that in the metabolism of the mold only very minute amounts of penicillin are formed and those only after days of growth. (One gm. of penicillin from 20 liters of culture fluid is a very high yield.) Difficulties have been encountered in selecting the most productive strains of the mold and the most suitable culture mediums, in developing methods

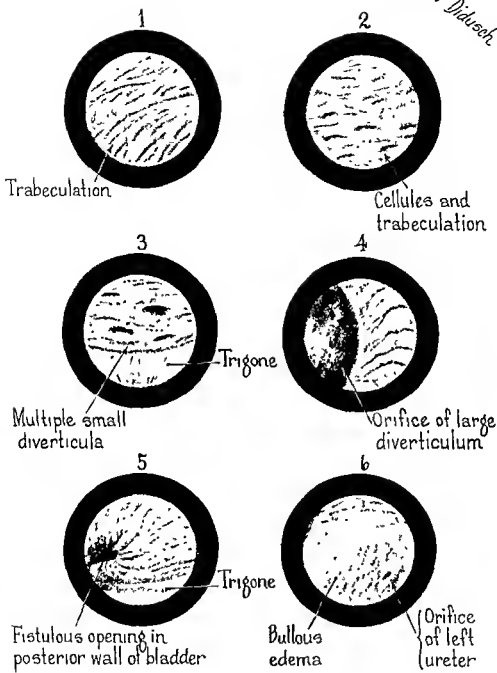


PLATE VII. CYSTOSCOPIC VIEWS

(1, 2) Trabeculation and cellules. (3, 4) Diverticula. (5) Fistulous opening in the bladder wall. (6) Bullous edema in the vicinity of the ureteral orifice.

of extracting and purifying the bacteria-killing substance, and in stabilizing the purified product.

The first clinical tests of penicillin in this country were reported by Dr. Martin H. Dawson, of Columbia University, in 1941. In June, 1942 the work of organizing and supervising clinical investigations in 22 selected hospitals was placed under the auspices of the Committee on Chemotherapeutic and Other Agents, of the National Research Council, the results to be collected and summarized by its chairman, Dr. Chester S. Keefer, Director of the Evans Memorial Hospital, in Boston. This Committee has recently reported the results obtained by these 22 groups of investigators in the treatment of 500 cases of various infections with penicillin; and it is upon this report that we have principally relied in the preparation of this section.

Owing to the small amounts of penicillin available for clinical investigation, the study thus far has been directed toward two groups of infections: (1) those that are most likely to occur in the armed forces, and (2) those that are resistant to the sulfonamides.

Modes of Administration: Preparation of Drug for Treatment. Penicillin can be given intravenously, intramuscularly, or topically. It is ineffective when given orally, probably because much of it is destroyed in the digestive process. The destructive action appears to be due to hydrochloric acid and not to pepsin. It is advisable to inject the drug directly into the subarachnoid space in meningitis, and into the pleural cavity in empyema.

Following intravenous or intramuscular injection, penicillin is excreted rapidly in the urine, so that in order to obtain an adequate amount of potent material in the blood and tissues it is necessary to inject the drug continuously or at frequent intervals (every 3 to 4 hours).

Penicillin is supplied in ampoules of 5,000 Oxford units, 10,000 units, 25,000 units, 100,000 units, and 1,000,000 units. As it is extremely soluble, it may be dissolved in small amounts of sterile, distilled, pyrogen-free water, in sterile isotonic solution of sodium chloride, or in 5 per cent dextrose solution.

For interval intravenous injection (directly into the rubber tubing through a syringe), the dry powder may be dissolved in sterile isotonic solution of sodium chloride in concentrations of 1,000 to 5,000 units per cc.

For constant intravenous therapy, the powder may be dissolved in sterile

saline solution in lower dilution—25 to 50 units per cc. The rate of delivery is regulated to between 75 and 100 cc. an hour.

For intramuscular injection, the total volume should be kept as low as possible—5,000 units per cc. of isotonic solution of sodium chloride—in order to avoid local soreness at the site of the injection.

For topical application, the powdered form of the sodium salt is irritating to wound surfaces and should not be used. Solutions in isotonic solution of sodium chloride, with a concentration of 250 units per cc. (500 units in more resistant infections) are satisfactory.

The total amount of penicillin, as well as the total amount given with each injection, the interval of time between injections, and the total duration of treatment, has varied greatly from one case to another, and no standard of treatment has as yet been laid down.

The "Oxford unit"—the system of measurement—is based upon comparison with standard material furnished by Oxford University to other laboratories. One million units weigh approximately one-fifth of an ounce; yet, so potent is the drug, that 100,000 units (one-fiftieth of an ounce) is often sufficient to cure a sulfonamide-resistant case of gonorrhea.

Absorption, Excretion, and Distribution. The absorption, excretion, and distribution of penicillin have been studied by Rammelkamp and Keefer, who summarized their findings as follows:

Intravenous injection of penicillin resulted in high initial concentration in the blood plasma, which was followed by an abrupt fall. Traces of penicillin were found in the blood for 30 to 210 minutes after the injection, the length of time depending on the amount administered. The sharp fall noted in the serum concentration immediately after the injection was associated with an increased excretion in the urine. The average excretion after intravenous injection was 58 per cent of the administered dose.

Penicillin was rapidly absorbed when given intramuscularly, and slowly absorbed after subcutaneous injections. Excretion in the urine was rapid following intramuscular injections and delayed after subcutaneous injections.

Absorption from the body cavities was delayed and was reflected in the slow excretion of penicillin by the kidneys. The total amount found in the urine was somewhat lower than that obtained following intravenous injection. Fluid aspirated from the pleural and joint cavities 22 and 13 hours after the injection showed appreciable amounts of penicillin remaining.

Administration of penicillin by enteral routes showed that absorption from the duodenum was rapid, whereas oral and rectal doses were poorly absorbed. These findings may be explained by the inactivating effect on penicillin of acid and *Escherichia coli*. After oral, intraduodenal and rectal administration, the average amount excreted in the urine was extremely small.

In the presence of renal failure penicillin was not excreted rapidly, and as a result high concentrations were maintained in the blood stream after intravenous injections.

Studies on the distribution of penicillin showed that the substance failed to penetrate the red cells in significant amounts. In general, the average concentration found in erythrocytes was less than 10 per cent of the plasma concentration. No penicillin was found in the spinal fluid, saliva or tears in subjects receiving it intravenously.

Infections Responsive to Penicillin: Dosage. Penicillin has been found to be most effective in the treatment of infections due to the *Staphylococcus aureus* (with and without bacteriemia), gonococcus, pneumococcus, and *Streptococcus hemolyticus*. It has been tested most extensively in the treatment of staphylococcic and gonococcic infections. It is a powerful weapon against osteomyelitis, empyema, boils and carbuncles, mastoiditis, meningitis, cellulitis, pneumonia, and the infections that follow burns. Experimentally it is a potent agent in gas bacillus infections. It has been of great benefit in infections that are resistant to the sulfonamides.

Penicillin has proved ineffective against bacterial endocarditis. It is also valueless against tuberculosis; and there is little likelihood that it will work against such virus diseases as infantile paralysis or yellow fever. It must be remembered that there are many infections against which penicillin has not yet been tried.

Dosage of the new drug has varied greatly from case to case due to the limited supply of the drug and because little is known about the best dosage for some infections. It has been definitely shown, however, that to obtain the best results it is necessary to inject the drug continuously or at frequent intervals for at least 7 to 14 days because of its very rapid excretion in the urine. Generally speaking, for serious staphylococcic infections a total of between 500,000 and 1,000,000 Oxford units, intravenously or intramuscularly injected, is required, and the best results have been obtained when treatment is continued for at least 10 to 14 days. At least 10,000 units should be given every 2 to 3 hours at the beginning of treatment, either by continuous intravenous or interval intravenous or intramuscular injections. Patients with pneumococcic pneumonia often recover following the use of 100,000 units given over a period of 3 days, while others require between 60,000 and 90,000 units daily for 4 to 7 days.

Penicillin in Sulfonamide-resistant Gonorrheal Infections. The most striking results of penicillin therapy have been in sulfonamide-resistant gonococcic infections. Of the 129 cases reviewed in the report of the Committee on Chemotherapeutic and Other Agents, most of which were treated by Dr. J. F. Maloney and his associates of the U. S. Public Health

Service, 125 were asymptomatic and bacteriologically negative in 9 to 48 hours after treatment with between 100,000 and 160,000 units. The dosage varied from 10,000 units every 3 hours for sixteen doses to 20,000 units every 3 hours for five doses or 25,000 units every 3 hours for three doses. The results of treatment should be controlled by culture of the exudate. The report states:

Here, then, is a most potent weapon in the treatment of sulfonamide-resistant gonorrhea, and it is not too much to predict that penicillin will prove to be one of the most effective agents in the treatment of a disease that causes great ineffectiveness in the armed forces and in the civilian population.

Toxic Reactions. Toxic reactions, common in treatment with the sulfonamides and many other drugs, have been rare with penicillin, despite the fact that only a small percentage of the substance available for clinical testing has been pure penicillin. In the 500 cases covered by the Committee's report, chills occurred in 12 and low-grade fever in 5; these were transitory and caused no difficulty. Urticarial eruptions occurred in 14; their cause is obscure. Thrombophlebitis at the site of injection was reported in 19 cases; this is more likely to occur when injections are made repeatedly and when concentrated solutions are used. Fleeting attacks of headache, flushing of the face, and muscle pains observed in some cases were evidently due to toxic substances, in earlier lots of the drug, carried over from the extraction process.

Nitrohydrochloric Acid in the Treatment of Colon Bacillus Infections

Crance and Maloney (1935) proposed a simple method of changing the urine to an acid reaction by the administration of nitrohydrochloric acid. This treatment, which was put forth by its proponents as a substitute for the efficient but unwieldy and unpleasant ketogenic diet, is effective in a high percentage of infections due to the *Escherichia coli*, which is destroyed in an acidity of from 5.1 to 4.6. Nitrohydrochloric acid reduces the pH of the urine to 5.3 or below in less time than the ketogenic diet and can be administered without hospitalization and without change in the ordinary diet. Tests have failed to show any renal damage, and no objections or contraindications to its use have been found.

The formula of Crance and Maloney is as follows:

Nitrohydrochloric acid (not the dilute)	Drams 4 ss (18 cc.)
Aqua dest. q s.	Ounces 4 (120 cc.)

Sig :—Drams 1 (4 cc) in $\frac{1}{3}$ glass of water followed by a full glass of water after meals and late at night.

Medication should be continued for one week after cultures become sterile. A pH of 5.1 is necessary to obtain satisfactory results. A careful check should be kept on the pH by the use of a standard pH comparator.

Diet

The question of diet is an important one in the treatment of vesical inflammations. Certain forms of infection call for specific diets to reinforce the effects of the therapeutic measures that are being applied to combat the infection. Diet also has an important place in the treatment of urinary stone and tuberculosis.

KETOGENIC DIET

The ketogenic diet was introduced in 1931 by Clark and Helmholz, of the Mayo Clinic, working independently. Remarkable results have been claimed for it in the treatment of infections of the bladder and upper urinary tract due to *Escherichia coli*. Its use produces a highly acid urine and a substance which definitely inhibits the growth of certain microorganisms. Fuller (1933) showed that levorotary beta-hydroxy-butyric acid is the ketone body producing the bacteriostatic effect. A sufficient concentration of ketone bodies in a urine of pH 5.5 or less is effective in eradicating the colon bacillus infection.

B. pyocyaneus infections respond well to the ketogenic diet, as do the majority of the remaining types of organisms found in bacillurias with the exception of the aerogenous type of colon bacillus.

Crance has pointed out that when the colon bacillus has been determined to be the offending organism, the specimen should be subcultured to determine which of two types of colon bacilli is present before treatment by the ketogenic regimen is attempted. The *Escherichia coli*, which represents about 75 per cent of colon bacillus infections of the urinary tract, is much more amenable to treatment by the ketogenic diet than the aerogenous type, which has thus far failed to respond to treatment by this method in a sufficient number of cases to warrant the submitting of patients to hospitalization or dietary measures. The two types are easily differentiated. The aerogenous type produces gas within 48 hours in saccharose, whereas *Escherichia coli* does not. Both types form gas in lactose.

In order to obtain successful results, the bacteriostatic effect must be continuous and maintained as uniformly maximum as possible during the entire 24 hours. Ketosis should develop within 3 to 5 days and a

normal diet resumed at the end of 10 to 12 days. Several short courses are preferable to one long course.

If the acidity of the urine is above pH 5.2 when the ketone bodies have appeared in the urine, it may be advisable to give ammonium chloride orally to increase its acidity. This may be given in enteric coated tablets. If, on the other hand, sufficient acidity has developed, but the percentage of ketone bodies in the urine is insufficient to produce the necessary bacteriostatic action, the oral administration of methenamine may increase the bacteriostatic power of the urine to a point at which the organism will be eliminated.

Herrold's method for determining the approximate acidity of the urine is rapid and easily performed. A drop of chlor-phenol red is added to 20 drops of freshly voided urine. If there is no change in the color of the urine, the pH is about 5.4, which is the right degree of acidity to permit the ketone bodies to exert their bactericidal powers. Pink or deep red urine, after addition of the indicator, means that the acidity is above pH 5.4, and the urine is, therefore, insufficiently acid. If the urine is allowed to stand even for a comparatively short time, the urea-splitting organisms which it contains will increase the pH .

The ferric-chloride test for diacetic acid is a simple test for determination of the concentration of ketone bodies in the urine. To 10 cc. of urine add an equal volume of a 10 per cent aqueous solution of ferric-chloride. If a Bordeaux-red color develops, diacetic acid is present in the urine.

Although the ketogenic diet has proved its efficiency in the treatment of *Escherichia coli* and other bacillurias in many instances, it has several serious drawbacks. It requires rigid supervision, and hospitalization is usually necessary for its successful carrying out. It often causes distressing general and gastrointestinal symptoms, and it is difficult to persuade patients to take it. Since the bacteriostatic agent must be eliminated by the kidneys, poor renal function is a contraindication for this type of treatment.

In brief, the ketogenic diet consists of the administration of a large amount of fat, with insufficient carbohydrates to burn the fat completely, and an amount of protein normal to the patient under treatment. The fat is only partly oxidized, due to insufficient glucose, causing ketone bodies to be thrown off in the urine. The highly acid ketone urine has antiseptic properties. The diet is an inadequate diet, low in minerals and vitamins, normal in protein and calories, high in fat, and very low in carbohydrates.

Normal intake of fluids should be encouraged, but the forcing of fluids is discontinued for the duration of the diet.

A typical ketogenic diet for a patient weighing 150 pounds is given in Table VIII. The diet contains approximately 45 grams protein, 235 grams fat, 20 grams carbohydrate (2375 calories). The available glucose is 54 grams, and the ketogenic antiketogenic ratio approximately 4.3 to 1.

TABLE VIII

MORNING	NOON	NIGHT
2 eggs	1½ ounces medium fat meat, fish, or fowl (45 grams)	1 egg or 1 ounce medium fat meat (30 grams)
3 strips cooked bacon 3 inches long (10 grams)	½ cup 3% vegetable (100 grams)	½ cup 3% vegetable (150 grams)
¼ glass 40% cream (150 grams)	½ glass 40% cream (150 grams)	½ glass 40% cream (150 grams)
½ cup 3% fruit or vegetable (100 grams)	2 teaspoons butter (10 grams)	3 teaspoons butter (15 grams)
2 teaspoons butter (10 grams)	Tea	Tea
Coffee		
Saccharine		

TABLE IX

MORNING	NOON	NIGHT
2 eggs	Broth	1 egg or 1 ounce medium fat meat (30 grams)
½ cup 3% fruit or vegetable (100 grams)	2 ounces medium fat meat (60 grams)	1½ cups 3% vegetable (300 grams)
3 strips cooked bacon, 3 inches long (10 grams)	1 cup 3% vegetable (200 grams)	1 tablespoon 40% cream (15 grams)
2 teaspoons butter (10 grams)	1 tablespoon 40% cream (15 grams)	1 teaspoon butter (5 grams)
1 tablespoon 40% cream (15 grams)	2 teaspoons butter (10 grams)	Tea
Coffee	Tea	
Saccharine		

Since many patients find it difficult to take the ordinary high fat ketogenic diet, a low caloric ketogenic diet—that is, a diet normal in protein ($\frac{2}{3}$ gram per kilogram of body weight), low in carbohydrate ($\frac{1}{10}$ gram per kilogram), and with enough fat to be palatable—is recommended. The diet is low in calories and available glucose, and depends on the burning of the patient's own body fat to produce ketosis.

A typical low caloric ketogenic diet for a patient weighing 150 pounds is given in Table IX. The diet contains approximately 45 grams protein, 75 grams fat, 20 grams carbohydrate (935 calories). The avail-

able glucose is 46 grams, and the ketogenic antiketogenic ratio approximately 4.3 to 1.

HIGH ACID ASH DIET

The high acid ash diet is used in the treatment of certain types of urinary calculus and other conditions in which it is deemed advisable to change the reaction of the urine, making it acid. The diet contains foods in such proportion that there will be an excess of acid ash produced.

The following foods are restricted in the diet:

Milk	1 pint daily
Fruits	} Not to exceed 25 points daily. See list.
Vegetables	

The following foods are included in the diet daily:

Cereal: 1 serving
 Bread (dark) 4 slices
 Meat, fish, chicken, or American cheddar cheese: 2 large servings
 Eggs: 2
 Macaroni, spaghetti, noodles, or rice: 1 serving

In addition to the above, the following foods may be eaten as desired:

Plain cookies, plain cake, pastry made with custard or allowed amounts of fruit fillings, unsalted popcorn, candy, English walnuts, unsalted peanuts, unsalted crackers, sweet butter, oil, mayonnaise, sugar, tapioca, unsalted gravy, unsalted broth, tea, coffee, flour, cornstarch, gelatin, vanilla ice cream, and cream (sweet and sour)

The following foods are omitted from the diet:

Meat cured in salt, as bacon, ham, or salty fish
 Salted crackers
 Salted butter
 Chocolate

A small amount of salt may be used in cooking, but none is to be added at the table.

Fruits and vegetables are chosen from the following lists only. Any combination of fruits and vegetables may be selected, but the total excess alkaline ash in the selected combination must not exceed 25 points daily.

Fruits	Amount	Points of Alkaline Ash
Blueberries	$\frac{1}{2}$ cup	2.7
Watermelon	$2\frac{1}{2}" \times 2\frac{1}{2}" \times \frac{1}{2}"$	2.7
Grapes	$\frac{1}{2}$ cup or 24 grapes	2.7
Pear	1 medium	3.6

Fruits	Amount	Points of Alkaline Ash
Apple	1 small	3.7
Grape juice	$\frac{1}{2}$ cup	3.9
Lemon juice	$\frac{1}{2}$ cup	4.1
Grapefruit	$\frac{1}{2}$	4.2
Cherry juice	$\frac{1}{2}$ cup	4.4
Orange juice	$\frac{1}{2}$ cup	4.5
Raspberry juice	$\frac{1}{2}$ cup	4.9
Peach	1 medium	5.0
Lemon	1 medium	5.5
Banana	$\frac{3}{4}$ cup or $\frac{1}{2}$ large	5.6
Orange	1 medium	5.6
Cherries	$\frac{3}{4}$ cup	6.1
Strawberries	10	6.6
Raspberries	$\frac{1}{2}$ cup-1 cup	6.7
Blackberries	$\frac{3}{4}$ cup-1 cup	6.7
Apricots	2 medium	6.8
Pineapple	$\frac{1}{2}$ cup diced	6.8
Muskmelon or cantaloupe	$\frac{1}{2}$ cup	7.5
Rhubarb	$\frac{1}{2}$ cup	8.6
Plums	As desired	Acid
Prunes	As desired	Acid
Cranberries	As desired	Acid
Vegetables	Amount	Points of Alkaline Ash
Asparagus	$\frac{1}{2}$ cup	0.8
Green peas	$\frac{3}{4}$ cup	1.3
Onions	$\frac{1}{2}$ cup	1.5
Pumpkins	$\frac{1}{2}$ cup cooked	1.5
Eggplant	$\frac{1}{2}$ cup cooked	2.2
Turnips	$\frac{1}{2}$ cup cooked	2.7
Squash	$\frac{1}{2}$ cup mashed	2.8
Radishes	10	2.9
Mushrooms	$\frac{1}{2}$ cup canned	4.0
Broccoli	$\frac{1}{2}$ cup scant	5.2
Cauliflower	$\frac{1}{2}$ cup cooked	5.3
String beans	$\frac{3}{4}$ cup cooked	5.4
Tomatoes	$\frac{1}{2}$ cup	5.6
Cabbage	$\frac{1}{2}$ cup cooked; $1\frac{1}{2}$ cup raw	6.0
Tomato juice	$\frac{1}{2}$ cup	6.2
Sweet potato	$\frac{1}{2}$ medium	6.7
White potato	1 potato $2\frac{1}{2}$ " diameter	7.0
Lettuce	$\frac{1}{2}$ head or 16 leaves	7.4
Kale	$\frac{1}{2}$ cup cooked	7.6
Celery	4 stalks or $\frac{1}{2}$ cup	7.8
Cucumbers	$\frac{1}{2}$ cup sliced	7.9
Rutabagas	$\frac{1}{2}$ cup mashed	8.5
Carrots	$\frac{3}{4}$ cup	10.8
Beets	$\frac{3}{4}$ cup	10.9
Corn	As desired	Acid

(Sample Outline)

Morning	Noon	Night
Orange or grapefruit juice, $\frac{1}{2}$ cup	Meat, fish, or cheddar cheese	Meat, unsalted gravy
Cereal with sugar and $\frac{1}{2}$ glass milk	Vegetables (choose from list)	Rice, noodles, macaroni, or corn
Dark toast, 1 slice	Dark bread, sweet butter	Vegetables (choose from list)
Sweet butter	Salad (choose from list)	Dark bread, sweet butter
Egg, 1	Dessert	Fruit (choose from list)
Coffee, cream, sugar	Milk, $\frac{1}{2}$ glass	Milk, $\frac{1}{2}$ glass
	3:00 p.m.	8:00 p.m.
	Custard	Eggnog ($\frac{1}{2}$ glass milk, 1 egg, sugar)
	Toast or unsalted crackers, sweet butter	Plain cookies or crackers

HIGH ALKALINE ASH DIET

The high alkaline ash diet is used in the treatment of certain cases of urinary calculus and other conditions (*i.e.*, acute cystitis, with dysuria) where it is deemed advisable to change the reaction of the urine, making it alkaline. The diet contains foods in such proportion that an excess of alkaline ash is produced.

The following foods are included in the diet:

Milk: 1 quart or more daily

Eggs and Meat: 3 small servings of meat or eggs a week and 3 strips of crisp bacon twice a week

Soup: Cream soup only

Fat: Any oil or fat; butter as desired

Cereal. 1 serving daily of any of the following: cornflakes, cornmeal, farina, puffed rice, puffed wheat, oatmeal

Bread: 3 slices daily, dark preferred

Vegetable: At least 4 servings daily. Omit corn and lentils.

Fruit At least 4 servings daily. Omit prunes, plums, and cranberries.

Salad: Any kind made of the fruits and vegetables allowed, daily.

Dessert: 1 serving daily of the following: ice-cream, ices, gelatin, junket (vanilla, chocolate, coffee, caramel, or fruit flavors allowed on fruit list)

Sugar: Any kind

Beverages: Coffee, tea, cocoa. With each meal include 1 glass of orange, pineapple, grapefruit juice or lemonade (containing juice of 1 lemon).

Nuts Almonds, chestnuts, cocoanut

Miscellaneous: Cornstarch, jam, jelly, and marmalade from fruits allowed, molasses, tapioca

The following foods are omitted from the diet:

Meat broths and all soups made with meat broth

(Sample Outline)

Morning	Noon	Night	8:00 p.m.
Fruit	Soup	Meat or eggs or bacon	Milk, 1 glass
Cereal	Potato	Potato	Fruit
Toast, 1 slice	Vegetable	Vegetables	
Butter	Salad	Salad	
Milk, 1 glass	Fruit	Fruit or dessert	
Fruit juice	Bread, 1 slice	Bread, 1 slice	
Coffee with cream, sugar	Butter	Butter	
	Milk, 1 glass	Milk, 1 glass	
	Fruit juice, 1 glass	Fruit juice, 1 glass	

BRADY MODIFIED ALKALINE ASH DIET

The Brady modified alkaline ash diet is used in the treatment of inoperable and postoperative urogenital tuberculosis with bladder irritation. The diet lessens the acidity of the urine. It excludes foods which are generally irritating to the diseased urogenital tract, and serves as a basis for developing a diet adapted to individual idiosyncrasies. The diet contains foods in such proportion that an excess of alkaline ash is produced.

This diet fulfills adequately the normal food requirements with the exception of iron. Due to the elimination of eggs and the restriction of meats, the iron content of the diet falls below the normal requirement of .015 grams. In order to meet the need in so far as possible, fruits and vegetables high in iron should be included in large amounts. This diet contains approximately 75 grams protein, 85 grams fat, 280 grams carbohydrate (2,200 calories).

The following foods are included in the diet:

Milk: 1 quart or more of sweet milk daily

Meat: 3 lamb chops or 3 $\frac{1}{2}$ ounce servings of lamb a week and 3 strips of crisp bacon twice a week

Soup: Cream soup only

Fat: Any oil or fat

Cereal: 1 serving daily of any of the following: cornflakes, cornmeal, farina, puffed rice, puffed wheat, cornmeal

Bread: 3 slices daily, dark preferred

Vegetable: At least 4 servings daily with the exceptions noted below

Fruit: At least 4 servings daily with the exceptions noted below

Salad: Any kind made of the fruits and vegetables allowed

Dessert: 1 serving daily of any of the following: ice-cream, ices, gelatin, junket; vanilla chocolate, coffee, caramel, or fruit flavors allowed on the fruit list

Sugar: Any kind

Beverage: With each meal include 1 glass of orange or pineapple juice or lemonade (containing juice of 1 lemon); coffee, 1 cup daily; cocoa, in moderate amounts

Nuts: Almonds, chestnuts, cocoanut

Miscellaneous: Cornstarch, jams, jelly, and marmalade from fruits as allowed, molasses, tapioca, salt in moderate amounts

The following foods are omitted from the list:

Milk: Sour milk and cream, buttermilk

Eggs

Cheese

Soup: Meat broth and all soups made with meat broth

Vegetable: Corn, lentils, asparagus, broccoli, carrots, peppers, sauerkraut, tomatoes

Fruit: Prunes, plums, cranberries, apricots, berries, cherries, grapes, grapefruit, rhubarb

Beverages: Tea, alcoholic, fermented, and carbonated beverages

Miscellaneous: Condiments, pickles, fried foods

(Sample Outline)

Morning	Noon	Night	8:00 p m.
Fruit	Meat	Soup	Milk
Cereal	Potato	Potato	Fruit
Toast	Vegetable	Vegetable	
Butter	Salad	Salad	
Milk	Fruit or dessert	Fruit	
Cream	Bread	Bread	
Fruit juice	Butter	Butter	
Coffee	Milk	Milk	
Sugar	Fruit juice	Fruit juice	

LOW OXALATE DIET

A low oxalate diet is used in the treatment of calcium oxalate urinary stones. The diet is a general one with certain omissions and restrictions.

The following foods are omitted because of their high oxalic acid content:

Asparagus	Cranberries	Black tea
Beet greens	Figs	Chocolate
Spinach	Gooseberries	Cocoa
Sorrel	Plums	Gelatin
Dandelion greens	Rhubarb	Pepper
	Raspberries	

The following foods are restricted because of their moderate oxalic acid content:

Milk: 1 pint

Coffee: 1 cup

Pineapple

Orange

Strawberries

Tomatoes

Beets

Potatoes

Beans

Brussels sprouts

Not more than 1 serving daily from this group of fruits and vegetables

Low Calcium Modification

Cheese and cauliflower are omitted from the low oxalate diet, and milk is restricted to 1 pint daily.

Subarachnoid Injections of Alcohol for Vesical Pain

The intraspinal (subarachnoid) injection of alcohol has been widely recommended for the relief of intractable pain in the bladder and elsewhere. The alcohol is introduced into the subarachnoid space through a lumbar-puncture needle, all the details and precautions necessary in lumbar puncture being rigidly observed. The patient's head must be kept lower than the part of the spine which is being injected, and he must remain in this position for 10 minutes after the needle is withdrawn. He is then turned on his back, and the foot of the bed is elevated from 4 to 8 inches. He remains thus for 2 hours, after which his head may be raised, but he must not sit upright for at least 4 hours after injection. It is usually necessary to catheterize the patient for the first 24 hours, and sedatives may be required to relieve the bladder pain until the alcohol injection begins to have its effect.

It may be some time before the full effect of the alcohol upon the nerves is experienced; but a large number of case reports testify to the good results this technic has achieved in postoperative and inoperable cases of bladder tumor, Hunner's ulcer, and other vesical lesions causing severe pain.

Vaccines

Autogenous vaccine therapy has been used to a considerable extent in the treatment of bacteriuria, but the results have not been remarkable. The best results appear to have been obtained in the treatment of colon bacillus infection, or mixed infections in which the colon bacillus predominates.

The course of treatment should cover about 5 weeks. The injections are given in accordance with the acuteness of the cystitis, the usual interval being 2 to 3 days.

Bacteriophage Therapy

Bacteriophage therapy, despite its very definite limitations, has been employed with considerable success in many cases of urinary-tract infection. The use of this agent is described under Bacteriophage Therapy of Infections of the Kidneys and Bladder (p. 1718).

Treatment of Inoperable and Postoperative Urogenital Tuberculosis

Following nephrectomy, or the removal of a tuberculous focus in the prostate or seminal vesicles, it frequently happens that the secondary lesions in the bladder heal spontaneously. In many cases, however, this happy outcome does not take place, and the unfortunate patient is left in as distressful a condition as before operation. The same situation, only more intensified, confronts the physician treating a case of inoperable bilateral renal tuberculosis. Some of the best minds in the urological profession have been struggling for years with this vexatious and exceedingly important problem.

At the Brady Foundation, in the New York Hospital, these patients are treated at a special clinic devoted entirely to the care of those suffering from inoperable or postoperative tuberculosis of the urogenital tract. This clinic is in the charge of Dr. Stanley L. Wang. The largest group of patients comprise those who either have undergone nephrectomy for unilateral renal tuberculosis, or have had the worse kidney removed in bilateral involvement. The inoperable renal patients fall into three groups: (1) those with bilateral renal tuberculosis about equally distributed in both kidneys, (2) those with unilateral lesions so slight that little kidney destruction is evident and nephrectomy is unwarranted, (3) those who refuse surgery and must, therefore, be treated as inoperable.

The plan of treatment now in use has been developed over a period of years. The treatment is based on the building up of a regimen to meet the needs of the individual patient. It is administered along two lines: (1) the urological, and (2) the constitutional treatment of tuberculosis (by rest, fresh air, diet, etc.). Urogenital tuberculosis is a local manifestation of a systemic disease; treatment must, therefore, aim at the patient as a whole, not only at the lesion in the urinary or genital tract. Frequently treatment must be carried out over long periods, sometimes for years. The results have been heartening, many patients showing marked constitutional and local improvement, and some actual cures.

The urological treatment varies with the many different aspects of the disease in the urogenital tract. In general, it includes (as indicated) bladder instillations, irrigations, and insufflations, renal pelvic lavage, prostatic and seminal vesicular treatments, fulguration of localized bladder ulcers, ureteral dilatations, and additional surgical measures as the need arises.

Belts are recommended to support the remaining kidney, which hyper-

trophies after nephrectomy. Severe pain due to ureteral kinks may occur if the belts are not worn for a year or more during waking hours.

Stricture of the intramural portion of the remaining ureter sometimes occurs in extensive vesical tuberculosis, and may even appear long after nephrectomy and arrest of the tuberculosis. Relief of symptoms is afforded by dilatations, which must, however, be continued indefinitely.

Tuberculosis of the bladder, which is probably always secondary to tuberculosis of the kidney or seminal tract, causes much suffering and inconvenience, and many remedies have been utilized in attempts to relieve it. Much depends on the condition of the bladder wall—whether it is widely involved and trabeculated—and if the capacity of the bladder is decreased. Some patients are unable to tolerate any form of local treatment, regardless of the extent of the disease in the bladder. Treatment is not always effective, but proper diet, internal medication, and local treatment usually give some degree of alleviation.

Instillations into the bladder of various substances have been found useful for relieving pain. These include oil of cajeput or gomenol, 2 per cent in olive-oil, warmed and instilled with a small soft-rubber catheter. The oil injections are best restricted to patients whose bladder walls have sufficient muscular tone to dispel the solution, so that it does not remain in the bladder indefinitely and cause increased irritation. Novocaine borate, 2 per cent is also useful. Filling the contracted bladder with a very dilute solution of bichloride of mercury (beginning with 1:75,000 and slowly increasing to 1:15,000 or 1:10,000) enlarges the vesical capacity and relieves pain in some instances.

Transurethral superficial fulguration of localized bladder ulcerations (under anesthesia) not only controls the bleeding but affords relief from the distressing bladder symptoms in many cases that have failed to respond to the ordinary hygienic methods of treatment.

The importance of the *constitutional treatment* of tuberculosis is emphasized to all patients. It consists of rest, fresh air, a special dietary regimen, old tuberculin, medicinal therapy, and quartz-light irradiation both externally and intravesically. The benefits derived are from the combination of these elements. Heliotherapy is indicated in all cases of genito-urinary tuberculosis without active lung lesions, but there are obvious limitations to its usage in urban localities. Whenever possible, patients are advised to take sun treatments on the days of the week when

they do not receive the lamp exposures, and are given exact instructions regarding the duration and extent of the exposures.

The patient is given minute instructions regarding rest, exercise, fresh air, and diet. His idiosyncrasies must often be considered and treatment adapted to them. Usually a high caloric, high vitamin diet is given. When there is present a tuberculous cystitis, with a painful, irritable bladder, the diet is modified by the exclusion of foods that are irritating to the diseased bladder mucosa. A modified high alkaline ash diet is useful as a starting-point, continuing or changing it with the pH of the urine as a guide (Brady Modified Alkaline Ash Diet, p. 1193).

Internal drugs include viosterol, haliver oil and viosterol, and cod-liver oil, methylene blue for burning on urination, and, for irritable bladder, Kirwin's Mixture:

Potassium citrate	Dr. 6 (24 cc.)
Tinct Hyoscyami	Oz. 1 (30 cc.)
Tinct Opii Camphorata	Oz. 1 (30 cc.)
Elix. saw Palmetto et Santalwood q s. ad.	Oz. 4 (120 cc.)
Sig.:—Dr 2 (8 cc.) q. 4 hrs.	

Dr. Stanley L. Wang, working in the Brady Foundation, at the New York Hospital, with parallel series of cases, has concluded, after more than 10 years of experimentation, that patients suffering from urogenital tuberculosis (in whom there are no demonstrable lung lesions), who have been treated with gradually increased doses of Koch's old tuberculin, do much better than those who live under the same excellent hygienic conditions without receiving the injections. Old tuberculin has distinct value as a form of stimulative therapy, particularly in postoperative cases where the active focus has been removed surgically and the convalescence tends to be sluggish. In active, progressive lesions there have been no good results from its use. The tuberculin is diluted with a diluent of 0.6 of 1 per cent sodium chloride, to which is added 0.25 of 1 per cent phenol. The dilutions are extended to 1 to 10 millions. Treatment is begun with 0.1 to 1 cc. of the 1 to 10-million dilution, given hypodermically twice each week. The dose is increased 0.1 of 1 cc. each dose until a local, focal, or general reaction ensues. When this occurs, the dosage is reduced to the starting-point of 0.1 to 1 cc. of the 1 to 10-million dilution and begun all over again. It is our practice to stop if reactions constantly occur to small doses, indicating probable supersensitiveness.

Quartz Light Therapy. Quartz light therapy—for general irradiation over the regions of the kidneys and bladder, for the local irradiation of

sinuses, and for intravesical irradiation—has been found a valuable adjunct in the treatment of inoperable and postoperative tuberculosis of the urogenital tract. The irradiations are not given alone, but as part of a general regimen of treatment.

Local irradiation with air-cooled mercury vapor quartz lamps is almost a specific in the treatment of the postoperative wounds and sinuses that so frequently delay recovery following nephrectomy, epididymectomy, seminal vesiculectomy, etc. Treatments are given twice each week, beginning with a one-minute exposure at a distance of 20 inches from the wound and increasing gradually to 7 minutes and slowly shortening the distance to 15 inches, continuing thus until healing ensues. Formerly, postnephrectomy sinuses frequently remained open for years, but with quartz lamp irradiations the average time of healing is a matter of months.

Similar exposures are given twice a week—sometimes for long periods of time—over the region of the kidney, bladder, epididymis, or testicle in all postoperative and inoperable cases presenting tuberculosis of these organs. The heat, as well as the light, of the lamps is utilized. In the postoperative cases the treatments are started 2 or 3 weeks after operation. The treatments are begun gradually and the lamp brought closer, depending on the skin reactions, until exposures of 7 or 8 minutes at a distance of 12 to 15 inches are being given.

Lowsley-Wang Lamp for Intravesical Irradiation and Treatment of Tuberculous Sinuses. Intravesical irradiations for tuberculous cystitis, by means of the Lowsley-Wang bladder lamp, have yielded decidedly beneficial results in many cases.

This is a quartz vapor mercury arc lamp of the vacuum discharge type, and differs mechanically and in its emission from the air-cooled mercury vapor quartz lamps. Mechanically, it is of the high voltage discharge mercury vapor type, and operates at a temperature sufficiently low that the heat of the electrode is barely felt on the skin or mucosa. The difference in the emission of the rays is clearly shown by the comparison of the two spectrums. The rays from the high voltage discharge mercury vapor lamp differ from the other in that they are of a monochromatic nature, since about 90 per cent are concentrated in the wave-length at 2,537 angstrom units.

The intravesical applicator (Fig. 274) is of fused quartz, readily transmitting the rays. It is about the same length and shape as a Brown-Buerger cystoscope and approximately No. 24-F. in diameter. There is

an extra tube built into the quartz, with an opening near the tip of the applicator and an extension at the other end for the attachment of a rubber tube. The tube is for the purpose of catheterizing the bladder. After the bladder is emptied of urine, air is insufflated through the tube with a syringe to distend the bladder slightly before irradiation. Following the treatment, an instillation can be made through the tube if desired. The applicator, with the exception of the part at the distal end, which protrudes into the bladder, is painted with a dark oak stain made with a

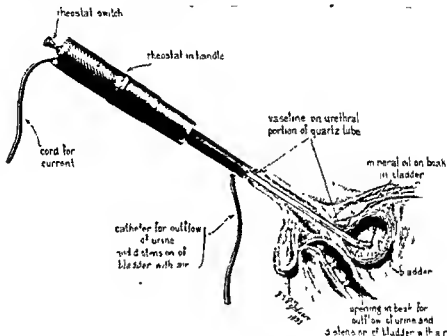


FIG. 274. Lowsley-Wang instrument for intravesical irradiation. Sagittal view of the bladder and urethra, with the instrument in place and the bladder distended with air for the dissemination of irradiation.

cellulose base to screen the rays from the urethra. When urethral irradiation is desired, the stain is easily removed with amyl acetate and can be reapplied when needed.

The instrument offers a simple and practical means of irradiating the interior of the bladder. At one operation, and in a very short time, the bladder can be emptied, then slightly distended with air and irradiated, and the air permitted to escape. The applicator passes easily through the urethra, and can be used equally well in male or female patients. A small amount of sterile liquid petrolatum, which permits the passage of the rays, is used on the tip of the applicator for lubrication.

The intravesical irradiations are given once each week. The exposures vary from 5 to 20 seconds, depending on the local reaction. The reactions are transitory, lasting for a few hours, and vary in accordance with the extent and sensitivity of the bladder lesions. Longer periods and more frequent treatments are unsatisfactory.

The bladder-lamp applicator is also frequently used for the irradiation of deep postoperative and other tuberculous sinuses. The narrow, rod-like shape of the applicator and the low heat adapt it to the irradiation of such wounds.

The instrument is sterilized in the formalin cabinet, and, when several patients are treated, is sterilized between applications by immersion of the applicator in oxycyanide of mercury, 1:1,000 for 10 minutes.

BIBLIOGRAPHY

- ABRAHAM, E. P., *et al.*: Further observations on penicillin. *Lancet*, 2: 177, 1941.
- ADAIR, F. L., DUNLAP, H., AND WILLMERT, G.: The mechanism of the action of pyridium. *J. Urol.*, 40: 319, 1938.
- ADAIR, F. L., AND HAG, L. R.: Sulfanilamide, sulfapyridine, sulfathiazole, and sulfadiazine therapy of gonorrhea. *New Engl. J. Med.*, 227: 465, 1942.
- AJAMIL, L. F.: Staphylo-streptococci ureterocystitis, and its treatment with sulfanilamide. *Urol. & Cutan. Rev.*, 41: 837, 1937.
- ALYEA, E. P.: Sulfathiazole therapy in urinary-tract infections. *J. Urol.*, 47: 219, 1942.
- ALYEA, E. P., AND ROBERTS, L. C.: Chemotherapy in non-specific infections of the urinary tract. *J. A. M. A.*, 115: 1345, 1940.
- ALYEA, E. P., AND STEWART, C.: Sulfathiazole and sulfadiazine therapy in urinary-tract infections. *Southern M. J.*, 34: 993, 1941.
- BEER, EDWIN: Removal of neoplasms of the urinary bladder. A new method employing high-frequency (Oudin) currents through a catheterizing cystoscope. *J. A. M. A.*, 54: 1768, 1910.
- BEER, EDWIN: Surgery of bladder tumors. *Ann. Surg.*, 101: 1412, 1935.
- BEER, EDWIN: Total cystectomy for infiltrating carcinoma of the bladder. *Am. J. Surg.*, 38: 192, 1937.
- BRATTON, A. C., AND MARSHALL, E. K., JR.: A new coupling component for sulfanilamide determinations. *J. Biol. Chem.*, 128: 537, 1939.
- BUCHTEL, H. A., AND COOK, E. N.: The use of sulfanilamide in the treatment of urinary infections. *Proc. Staff Meet., Mayo Clin.*, 12: 441, 1937.
- CAPORALE, LUIGI: Disturbance of micturition due to lesion of the nervous system. Read before the 18th Congress of the Italian Urol. Soc., Naples, November 1939.
- CARROLL, G., *et al.*: Sulfathiazole and staphylococcus in urinary infection. *J. Urol.*, 45: 770, 1941.
- CARROLL, G., *et al.*: Sodium sulfathiazole: a clinical study. *J. Urol.*, 47: 209, 1942.
- CARROLL, G., AND KAPPEL, L.: Granulocytopenia following use of sulfathiazole. *Urol. & Cutan. Rev.*, 54: 749, 1941.
- CARROLL, G., LEWIS, R., AND KAPPEL, L.: Mandelic acid as urinary antiseptic. *J. A. M. A.*, 107: 1798, 1936.
- CARROLL, G., LEWIS, B., AND KAPPEL, L.: Further clinical and laboratory observations of ruandelic acid. *J. Urol.*, 39: 710, May 1938.

- CAULK, J. R.: Litholapaxy: the method of preference for the removal of vesical calculi. *Trans Southern Surg Assoc.*, 43: 302, 1931.
- CAULK, J. R., AND EWERHARDT, F. H.: Direct internal irradiation of ultraviolet to the bladder. *Arch. Phys. Therapy*, 13: 325, 1932.
- CLARK, A. L.: Present status of dietary regimens in urinary infections. *J. A. M. A.*, 107: 1280, 1937.
- CLARK, A. L., AND KELTZ, B. F.: A simplified treatment of bacilluria. *J. A. M. A.*, 104: 289, 1935.
- COLEBROOK, L., AND KENNY, M.: Treatment of human puerperal infections, and of experimental infections in mice, with protosol. *Lancet*, 1: 1279, 1936.
- Committee on Chemotherapeutic and Other Agents, Division of Medical Sciences, National Research Council: Penicillin in the treatment of infections: report of 500 cases. *J. A. M. A.*, 122: 1217, August 28, 1943.
- COOK, EDWARD N.: Chemotherapy in infections of the urinary tract. *J. Urol.*, 39: 692, May 1938.
- COOK, EDWARD N.: Recent advances with chemotherapy in the treatment of infections of the urinary tract. *New Engl. J. Med.*, 226: 187, 1942.
- COOK, E. N., AND BUCHTEL, H. A.: Mandelic acid in the treatment of infections of the urinary tract. *J. A. M. A.*, 107: 1799, 1936.
- COTTÉ, GASTON: La sympathectomie hypogastrique a-t-elle sa place dans la thérapeutique gynécologique? *Presse Med.*, 33: 98, 1925.
- COTTÉ, GASTON: Resection du sympathétique pelvien. *Gynec. et Obst.*, 23: 233, 1931.
- COUNSELLER, V. S., AND BRAASCH, W. F.: Diathermy for carcinoma of the bladder. *Ann. Surg.*, 101: 1418, 1935.
- CRANCE, ALBERT M.: The necessity for the standardization of the treatment of bacilluria. *J. A. M. A.*, 104: 286, 1935.
- CRANCE, ALBERT M., AND MALONEY, THOMAS W.: A new acid medication in the treatment of bacilluria. *J. Urol.*, 33: 657, 1935.
- CRENSHAW, J. L., AND COOK, E. N.: Limitations, dangers, and failures of sulfanilamide in the treatment of urinary tract infections. *J. Urol.*, 41: 64, January 1939.
- CROSBIE, A. H.: Rupture of the urinary bladder. *J. Urol.*, 12: 431, 1924.
- CULVER, H., AND SEIFERT, W. F.: Urinary antiseptics. Collective review. *Abstr. Surg.*, 70: 574, 1940.
- DAVIS, ALBERT: Technic of resection of presacral nerve. *Brit. J. Surg.*, 20: 516, 1933.
- DAVIS, EDWIN: Urinary antiseptics: a study of the antiseptic properties and the renal excretion of compounds related to phenolsulphonephthalein. Preliminary report. *J. A. M. A.*, 70: 581, 1918.
- DAVIS, EDWIN, AND SHARPE, J. C.: A comparison of methenamine, caprokol, pyridium, and acriflavine as to clinical efficiency. *J. A. M. A.*, 99: 2097, 1932.
- DEAKIN, R., AND PATON, J. F.: Sulfathiazole in the treatment of 200 cases of male gonorrhea. *J. Urol.*, 46: 1043, 1941.
- DEES, J. E., AND COLSTON, J. A. C.: The use of sulfanilamide in gonococcal infections. *J. A. M. A.*, 108: 1855, 1937.
- DENNIG, HELMUT: Die innervation der harnblase. Berlin, Julius Springer, 1926.
- DOMAGK, G.: Ein beitrage zur chemotherapie der bakteriellen infektionen. *Deutsche med. Wchnschr.*, 61: 250, 1935.
- DONOHUE, C. D.: Use of powdered sulfanilamide in infected genito-urinary wounds. *J. Urol.*, 46: 562, 1941.
- DOUGLASS, H. L.: Excision of the superior hypogastric plexus in the treatment of intractable interstitial cystitis. *Am. J. Surg.*, 25: 249, 1934.
- DUCOUDRAY, L.: Le santalol dans le traitement de la blennorrhagie. Paris Thèse, 1900.

- EBERBACH, C. W., AND ARN, R. D.: Hexylresorcinol in urinary-tract infections. J. A. M. A., 89: 512, 1927.
- ELAUT, L.: Surgical anatomy of so-called presacral nerve. Surg. Gynec. & Obst., 55: 581, 1932.
- FEINSTONE, W. H., *et al.*: Toxicity, absorption and chemotherapeutic activity of 2-sulfanilamidopyrimidine (sulfadiazine). Bull. Johns Hopkins Hosp., 67: 427, 1940.
- FINLAND, M., *et al.*: Sulfadiazine: therapeutic evaluation and toxic effects, etc. J. A. M. A., 116: 2641, 1941.
- FINLAND, M., *et al.*: Sulfadiazine: further clinical studies of its efficiency and toxic effects in 460 patients. Ann. Int. Med., 17: 920, 1942.
- FIROR, W. M., AND POTH, E. J.: Intestinal antiseptics, with special reference to sulfanilylguanidine. Ann. Surg., 114: 663, 1941.
- FOX, C. L., JR., JENSEN, O. J., JR., AND MCDGE, G. H.: The prevention of renal obstruction during sulfadiazine therapy. J. A. M. A., 121: 1147, 1943.
- FRANK, R. T.: Treatment of vesicovaginal fistula. J. Mt. Sinai Hosp., 4: 803, March-April 1938.
- FULLER, A. T.: The nature of the bactericidal substance in the urine of patients receiving a ketogenic diet. Biochem. J., 37: 976, 1933.
- GILLESPIE, J. B.: Experiments on the antibacterial properties of pyridium and serenium. Proc. Staff Meet., Mayo Clin., 7: 372, 1932.
- GILLIGAN, D. R., *et al.*: Prevention of crystalluria during sulfadiazine therapy. Proc. Soc. Exper. Biol. & Med., 102: 248, 1943.
- GRAVES, R. C., AND DRESSER, R.: Experiences with high-voltage roentgen therapy, etc., Trans. Am. Assoc. Genito-Urin. Surg., 30: 291, 1937.
- GREENE, L. F., POOL, T. L., AND COOK, E. N.: Sulfadiazine in the treatment of infections of the urinary tract. Proc. Staff Meet., Mayo Clin., 17: 509, 1942.
- HANZLIK, P. J., AND COLLINS, R. J.: Hexamethylenamin: the liberation of formaldehyde—the antiseptic efficiency under different chemical-biological conditions. Arch. Int. Med., 12: 578, 1913.
- HAYWARD, W. G.: Additional uses for tidal drainage. J. Urol., 46: 793, 1941.
- HELLWIG, C. A., AND REED, H. L.: Fatal anuria following sulfadiazine therapy. J. A. M. A., 119: 561, 1942.
- HELMHOLTZ, H. F.: The ketogenic diet in the treatment of pyuria of children with anomalies of the urinary tract. Proc. Staff Mtg., Mayo Clinic, 6: 606, 1931.
- HELMHOLTZ, H. F.: A comparison of mandelic acid and sulfanilamide as urinary antiseptics. J. A. M. A., 109: 1039, 1937.
- HELMHOLTZ, H. F.: Bacterial power of the urine after the administration of prontosil by mouth. Proc. Staff Meet., Mayo Clin., 12: 244, 1937.
- HELMHOLTZ, H. F.: The effectiveness of methenamine as a urinary antiseptic at various hydrogen ion concentrations. Proc. Mayo Clin., 7: 374, 1932.
- HELMHOLTZ, H. F.: The use of sulfathiazole as a urinary antiseptic. J. Urol., 45: 135, 1941.
- HELMHOLTZ, H. F.: A comparison of the bactericidal effect of low concentrations of sulfanilamide and sulfathiazole on bacteria from urinary infections. J. Urol., 46: 322, 1941.
- HELMHOLTZ, H. F.: Bacteriostatic action of sulfadiazine, sulfathiazole, sulfacetimide and sulfapyridine on bacteria isolated from infections. Proc. Staff Meet., Mayo Clin., 17: 529, 1942.
- HELMHOLTZ, H. F., AND OSTERBERG, A. E.: Rate of excretion and bactericidal power of mandelic acid in the urine. J. A. M. A., 117: 1794, 1936.
- HELMHOLTZ, H. F., AND OSTERBERG, A. E.: The bactericidal effect in urine of levorotary and racemic beta-oxibutyric acid. J. Urol., 35: 86, 1936.

- HENLINE, R. B.: Hexylresorcinol in the treatment of 50 cases of infections of the urinary tract. *J. Urol.*, 14: 119, 1925.
- HERRELL, W. E.: Use of penicillin in sulfonamide-resistant gonorrheal infections. *J. A. M. A.*, 122: 289, 1943.
- HESS, ELMER: Neuro-urological surgery. *Urol. & Cutan. Rev.*, 40: No. 3, 1936.
- HIGGINS, C. C.: Aseptic uretero-intestinal anastomosis. *Surg. Gynec. Obst.*, 57: 359, 1933. Also: *Am. J. Surg.*, 22: 207, 1933.
- HIGGINS, C. C.: Cystectomy and the transplantation of the ureters into the bowel for carcinoma of the bladder. *Surg. Gynec. Obst.*, 66: 549, February 1938.
- HIGGINS, C. C., AND SCHLUMBERGER, F. C.: Recent chemotherapeutic advances in the treatment of infections of the urinary tract. *Med. Clinics North Am.*, 22: 449, March 1938.
- HINMAN, FRANK: An experimental study of the antiseptic value in the urine of the internal use of hexamethylenamine. *J. A. M. A.*, 61: 1601, 1913.
- HUGHES, P. B., SAYEN, J. J., AND TOWSKY, L. W.: Sulfadiazine calculi in the urinary tract; report of case. *J. Urol.*, 47: 274, 1942.
- HYAMS, J. A., AND BUCHEL, H.: Modification of the Munro tidal drainage apparatus. *Am. J. Surg.*, 52: 86, 1941.
- LEWIN, W. K.: Operative treatment of stenosis of the vesical neck. *Brit. J. Surg.*, 26: No. 104, 1939.
- JABOULAY, M.: Le traitement de la nevralgie pelvienne par la paralysie du sympathique sacré. *Lyon méd.*, 90: 102, 1899.
- KEITZER, W. A., AND CAMPBELL, J. A.: Renal complications of sulfadiazine. *J. A. M. A.*, 119: 701, 1942.
- KELLY, H. A., AND DUMM, W. M.: Urinary incontinence in women, etc. *Surg. Gynec. Obst.*, 18: 444, 1914.
- KIRWIN, T. J.: The management of bladder tumors. *Surg. Gynec. Obst.*, 66: 998, June 1938.
- KIRWIN, T. J., AND LOWSLEY, O. S.: Radical relief of vesicovaginal fistula. *J. Urol.*, 33: 1, 1935.
- KOLMER, J. A.: Progress in chemotherapy of bacterial and other diseases, with special reference to the prontosils, sulfanilamide and sulfapyridine. *Arch. Int. Med.*, 65: 671, 1940.
- KULITZY, G.: Pyridium therapie bei entzündlichen erkrankungen der harnwege. *Zentralbl. f. Gynak.*, 57: 1777, 1933.
- LATARJET, A., AND BONNET, P.: Le plexus hypogastrique chez l'homme. *Lyon chir.*, 9: 619, 1913.
- LEARMONTH, J. R.: Resection of presacral nerve for cord bladder. *Proc. Staff Mtg. Mayo Clinic*, 5: 54, 1930.
- LEARMONTH, J. R.: Neurosurgery in the treatment of diseases of the urinary bladder. II. Treatment of vesical pain. *J. Urol.*, 26: 13, 1931.
- LEARMONTH, J. R.: Neurosurgery in the treatment of diseases of the urinary bladder. III. Treatment of certain types of vesical paralysis. *J. Urol.*, 26: 229, 1931.
- LEARMONTH, J. R.: Value of neurosurgery in certain vesical conditions. *J. A. M. A.*, 98: 633, 1932.
- LEONARD, V.: Secretion of bacterial urine and disinfection of the urinary tract following oral administration of certain alkyl derivatives of resorcinol. *J. A. M. A.*, 83: 2005, 1924.
- LEWIS, D. B.: Acute urinary retention due to crystallization of sulfadiazine. *Urol. & Cutan. Rev.*, 46: 372, 1942.
- LINDNER, H. J., AND ATCHESON, D. W.: Sulfathiazole and crystallization in the kidney. *J. Urol.*, 47: 262, 1942.

- LITTLE, S. C.: Nervous and mental effects of the sulfonamides. *J. A. M. A.*, 119: 467, 1942.
- LONG, P. H.: Clinical use of sulfanilamide, sulfapyridine, sulfathiazole, and sulfadiazine in the prophylaxis and treatment of infections. *Canad. M. J.*, 44: 217, 1941.
- LONG, P. H., AND BLISS, E. A.: Para-amino-benzene-sulfonamide and its derivatives: experimental and clinical observations on their use in the treatment of betahemolytic streptococci infection; preliminary report. *J. A. M. A.*, 108: 32, 1937.
- LONG, P. H., AND BLISS, E. A.: Clinical and experimental studies of sulfanilamide and sulfapyridine and related compounds. N. Y., The Macmillan Co., 1939.
- LOWER, W. E.: Disposition of the ureters in certain abdominal conditions of the urinary bladder. *J. A. M. A.*, 80: 1200, 1923.
- LOWSLEY, O. S.: Relief of congenital and traumatic incontinence of urine by operation. *J. A. M. A.*, 90: 511, 1928.
- LOWSLEY, O. S.: New operations for the relief of incontinence in both male and female. *J. Urol.*, 36: 400, 1936.
- LOWSLEY, O. S.: A new incision for operations upon the urinary bladder. *Am. J. Surg.*, 11: 305, 1931.
- LOWSLEY, O. S.: A new suction device (suprapubic suction cup). *Am. J. Surg.*, 27: 554, 1935.
- LOWSLEY, O. S., AND FORSYTHE, W. E., JR.: Urinary antiseptics. *Surg. Clin. North Amer.*, p. 410, April, 1940.
- LOWSLEY, O. S., AND GUTIERREZ, R.: Operative intervention for the relief of diverticulum of the urinary bladder: review of literature: analysis of 54 cases. *J. Urol.*, 19: 459, 1928.
- LOWSLEY, O. S., AND HUNT, ROBERT W.: A new operation for the relief of incontinence of urine and feces. *J. Urol.*, 41: 252, February 1939.
- LOWSLEY, O. S., AND KIRWIN, T. J.: Urology for Nurses, pp. 205-208. Phila., J. B. Lippincott Co., 1936.
- LOWSLEY, O. S., AND WANG, S. L.: A new instrument for intravesical irradiation. *Arch. Surg.*, 29: 85, 1934.
- LUBASH, S., AND TURKELL, J. H.: Hematuria with progressive oliguria due to ureteral obstruction following sulfathiazole administration. *N. Y. State J. Med.*, 43: 769, 1943.
- MACGOWAN, G.: The transverse incision and abdominal fascia, as a method of approach in suprapubic operations on the bladder and prostate. *J. A. M. A.*, 61: 1863, 1913.
- MACNEILL, A. E., AND BOWLER, J. P.: Irrigation and tidal drainage of the bladder. *New Engl. J. Med.*, 223: 128, 1940.
- MARSHALL, E. K.: Pharmacology of sulfanilamide. *J. Urol.*, 41: 8, January 1939.
- MASON, L. M.: Pyridium therapy in genito-urinary disease. *Virginia M. Monthly*, 58: 190, 1931.
- MATHÉ, C. P.: Sulfadiazine anuria due to mechanical blockage of the ureters by crystalline deposits: report of a case. *Urol. & Cutan. Rev.*, 47: 168, 1943.
- McSWAIN, B., AND GLENN, F.: Sulfadiazine in experimental streptococcal infection. *Arch. Surg.*, 44: 233, 1942.
- MULLER, G. P.: Surgical treatment of exstrophy of the bladder. *Surg. Clin. North Am.*, 15: 275, 1935.
- MUNRO, DONALD: "The cord bladder": its definition, treatment, and prognosis when associated with spinal injuries. *J. Urol.*, 36: 710, 1936.
- MUNRO, DONALD, AND HAHN, JOSEPH: Tidal drainage of the urinary bladder: preliminary report of this method of treatment as applied to "cord bladders," with a description of the apparatus. *New Engl. J. Med.*, 212: 229, 1935.
- MYERS, G. B., AND ROM, J.: Acute hemolytic anemia, hemoglobinuria and uremia following sulfanilamide. *Ann. Inter. Med.*, 14: 164, 1940-41.

- MYERS, H. C.: A simplified automatic intermittent irrigator. *Southern Surgeon*, 9: 193, 1940.
- MYLL, N. A.: Heliotherapy in the treatment of genito-urinary tuberculosis. *J. A. M. A.*, 82: 1834, 1924.
- NEGLEY, J. C.: Rupture of the bladder. *J. Urol.*, 18: 307, 1927.
- NESBIT, R. M., AND McDONNELL, C. H.: Low calory, low fat, ketogenic diet for the treatment of infections of the urinary tract. *J. A. M. A.*, 105: 1183, 1935.
- NETER, E.: Antibacterial activity of sulfadiazine toward *B. Coli* and enterococci isolated from patients with infections of the urinary tract. *J. Urol.*, 46: 95, 1941.
- NICOLAIER, A.: Ueber die therapeutische verwendung des hexamethylentetramin. *Centralbl. f. d. med. Wissensch.*, 32: 897, 1894.
- O'CONOR, V. J.: Functional incontinence in women; repair by a modification of Kelly's technic. *Surg. Clin. North Am.*, p. 205, 1931.
- PAGE, JOHN: The effect of neoarsphenamine in urinary infections. *Urol & Cutan. Rev.*, 42: 425, 1938.
- PETERSON, O. L., AND FINLAND, M.: Urinary tract in sulfonamide therapy. *Am. J. Med. Sci.*, 202: 757, 1941.
- PIERI, G.: Enervation ou ramisection. *Presse méd.*, 34: 72, 1926.
- PIERI, G.: Contributi clinici alla chirurgia del sistema nervoso vegetativo. *Arch. ital. di chir.*, 27: 454, 1930.
- PRANEUF, L. E.: Vesicovaginal fistula: management and end-results. *Am. J. Obst.*, 31: 316, 1936.
- PLUMMER, N., AND ENSWORTH, H. K.: Absorption and excretion of sulfadiazine. *Proc. Soc. Exper. Biol. & Med.*, 45: 734, 1940.
- POTH, E. J., *et al.*: Bacteriostatic properties of sulfanilamide and some of its derivatives. *Arch. Surg.*, 54: 187, 1942.
- PRENTISS, R. J., AND FLOCKS, R. H.: Complications from sulfanilamide therapy of urinary-tract infections. *J. Urol.*, 44: 377, 1940.
- PRESS, EDWARD, AND KENNERSTEIN, M.: Additional manifestations of sulfathiazole toxicity. *Arch. Dis Child*, 18: 50, 1943.
- PRIEN, E. L., CRABTREE, E. G., AND FROWDEL, C.: The mechanism of urinary-tract obstruction in sulfathiazole therapy. *J. Urol.*, 46: 1020, 1941.
- QUINBY, W. C.: Total cystectomy for cancer of the bladder. *Ann. Surg.*, 101: 1415, 1935.
- QUINBY, W. C.: Urologic aspects of vesicovaginal fistula. *New England M. J.*, 214: 415, 1936.
- RAMMELKAMP, C. H., AND KEEFER, C. S.: The absorption, excretion and distribution of penicillin. *J. Clin. Invest.*, 22: 425, 1943.
- RAMMELKAMP, C. H., AND MAXON, T.: Resistance of *Staphylococcus aureus* to the action of penicillin. *Proc. Soc. Exper. Biol. & Med.*, 51: 386, 1942.
- RAMMELKAMP, C. H., AND STONEBURNER, L.: Sulfathiazole: a clinical and in vitro study of its uses in infections of the urinary tract. *New Engl. J. Med.*, 224: 45, 1941.
- RANDALL, A., AND UHLE, C. A. W.: Transvesical diathermy in the treatment of cancer of the bladder. *Surg. Gynec. Obst.*, 66: 927, May 1938.
- RICHARDS, A. N.: Penicillin. *J. A. M. A.*, 122: 235, 1943.
- RICHES, E. W.: Some landmarks in the surgery of stone. *Brit. J. Urol.*, 7: 140, 1935.
- ROSENHEIM, M. L.: Mandelic acid in the treatment of urinary infections. *Lancet*, 1: 1033, 1935. Also: *New Internat. Clin.*, 2: 43, June 1938.
- SCHNOHR, E., AND JOHANSEN, C.: Treatment of infections of the renal tract with mandelic acid. *Hospitalstud.*, 80: 453, 1937.

- SCHROEDER, C. F., AND CUMMING, R. E.: Resection of superior hypogastric plexus and sacral sympathetic ganglions, for the relief of pain in the bladder. *J. A. M. A.*, 112 :390, February 4, 1939.
- SCHWARTZ, L., *et al.*: Effect of alkali on crystalluria from sulfathiazole and sulfadiazine. *J. A. M. A.*, 117: 514, 1941.
- SEGRÉ, M.: Il trattamento roentgen delle forme di tubercolosi vesicale cronica. *Radio med.*, 24: 139, 1937.
- SHOHL, A. T., AND DEMING, C. L.: Hexamethylenamin: its quantitative factors in therapy. *J. Urol.*, 4: 419, 1920.
- SIMON, J.: Ectopia vesicae, etc. *Lancet*, 2: 563, 1862.
- STEDMAN, H. E.: An induction motor suction pump for drainage in urologic cases. *J. Urol.*, 40: No. 2, August 1938.
- TAIT, J. T.: Urinary antiseptics: a critical survey. *Brit. M. J.*, 2: 1252, 1935.
- THACKSTON, L. P.: Transurethral removal of urinary calculi. *Urol. & Cutan. Rev.*, 39: 423, 1935.
- THOMAS, H. W.: Tidal drainage and tidal irrigation. *Urol. & Cutan. Rev.*, 45: 147, 1941.
- TRÉFOUËL, J., *et al.*: Activité du p-amino-phénysulfamide sur les infections streptococciques expérimentales de la souris et du lapin. *Compt. rend. Soc. de biol.*, 120: 756, 1935.
- TWINEM, F. P.: Clinical and experimental study of lithotripsy. *Am. J. Surg.*, 24: 34, 1936.
- TWINEM, F. P.: One hundred years of bladder stone surgery at the New York Hospital. *Urol. & Cutan. Rev.*, 42: 313, May 1938.
- WALTERS, WALTMAN: An omental flap in the transperitoneal repair of recurring vesicovaginal fistulas. *Surg. Gynec. & Obst.*, 64: 74, 1937.
- WALTERS, W., AND BRAASCH, W. F.: Ureteral transplantation to the rectosigmoid for exstrophy of the bladder, complete epispadias, and other urethral abnormalities with total urinary incontinence. *Am. J. Surg.*, 23: 255, February 1934.
- WALTHER, H. W. E.: Urinary antiseptics: historical review and present evaluation. *J. A. M. A.*, 109: 999, 1937.
- WANG, S. L.: The treatment of inoperable and postoperative urogenital tuberculosis. *Am. Rev. Tuberculosis*, 28: 746, 1935.
- WANG, S. L.: Quartz light therapy in urogenital tuberculosis. *J. A. M. A.*, 104: 720, 1935.
- WANG, S. L.: Medical care in the treatment of urogenital tuberculosis. *Urol. & Cutan. Rev.*, 46: 606, 1942.
- WEIL, GROVER C., *et al.*: The local therapeutic effect of sulfathiazole. *Am. J. Surg.*, 55: 374, 1942.
- WEINSTEIN, M. L., AND ADAMS, E. L.: Sulfathiazole anuria cured by decapsulation of the kidneys. *Am. J. Surg.*, 11: 105, 1943.
- WHEELER, C., AND PLUMMER, N.: Sulfadiazine and sodium sulfadiazine: a comparison of certain of their clinical and pharmacologic values. *Ann. Int. Med.*, 17: 269, 1942.
- WHITE, E. W.: Evaluation of surgical diathermy in the treatment of bladder tumors. *Urol. & Cutan. Rev.*, 42: 248, April 1938.
- WRIGHT, E. O., AND KINSEY, R. E.: Renal complications of sulfadiazine. *J. A. M. A.*, 120: 1351, 1942.
- YOUNG, H. H.: Excision of vesical diverticula after intravesical invagination by suction: a new method. *Surg. Gynec. Obst.*, 26: 125, 1918.
- YOUNG, H. H., *et al.*: Use of sulfathiazole before and after urologic operations to prevent or combat infection. *J. Urol.*, 44: 714, 1940.

CHAPTER XXXIII

EMBRYOLOGY, ANATOMY, ANOMALIES, AND PHYSIOLOGY OF THE URETER

The ureter is the excretory duct of the kidney, and serves to transport the urine from the renal pelvis to the bladder.

A. EMBRYOLOGY OF THE URETER

The ureter, renal pelvis, and collecting tubules, comprising the collecting system of the kidney, are developed separately from the secretory system. The collecting system arises from the ureteral bud, whereas the secreting portions of the kidney arise from the metanephrogenic blastema (Embryology of the Kidney, p. 1346).

During the fourth week (in embryos of 4.5 to 5 mm. greatest length) a small, tubular evagination appears on the dorsal wall of the mesonephric (wolffian) duct where it bends ventrally to form the cloaca. This is the *ureteral bud*, the anlage of the collecting system of the kidney. At first it grows dorsally toward the vertebral column, and becomes differentiated into two parts: a narrow stalk, which later becomes the ureter, and a dilated terminal portion, the forerunner of the renal pelvis and the collecting tubules. In embryos of 8.5 to 9.5 mm. the ureteral bud forms a curve, which gradually becomes flatter, and the ureter grows cranially between the vertebral column and the mesonephros.

The secreting portion of the kidney has its origin in a mass of mesodermal cells arising from the caudal portion of the nephrogenic cord. As the ureteral bud develops, it impinges upon the metanephrogenic tissue, which forms a cap on its dilated end. With elongation of the ureteral stalk the metanephrogenic cap is pushed dorsocranially until the ureteral bud lies in the mesoderm dorsal to the mesonephros in the region of the second lumbar segment. This is the definitive position of the renal pelvis, and it is reached in embryos of 9.5 to 13 mm. length. In order to maintain this position during growth of the body, the ureter, which connects the kidney with the mesonephric duct at first, and later with the cloaca and bladder, must elongate considerably. This elongation is the result of growth along the entire length of the ureter. When

the ureter has reached its full expansion, it extends through the length of 3 or 4 vertebrae (from the twelfth thoracic to the fourth lumbar). Usually the higher location of the left kidney is already observable in embryos of 22 mm.

When the embryo is from 8 to 10 mm. long, primary evaginations, representing the future calyces of the kidney, begin to grow out from the primitive renal pelvis into the metanephrogenic blastema. At first there are two of these *primary tubules*, a cranial and a caudal. Later two more tubules develop between them. The distal end of each primary tubule enlarges to form an ampulla, and from each ampulla two other evaginations develop, forming secondary tubules. These subsequently develop tertiary tubules, and this branching process continues until 12 or more divisions of tubules have formed. The cranial and caudal primary tubules develop into the *major calyces*, and the secondary tubules opening into them form the *minor calyces*. The tubules of the third and fourth generations are absorbed by the walls of the minor calyces. The tubules of the fifth order become the *papillary ducts*, and the remaining orders elongate and become the *collecting tubules* of the renal pyramids.

This process of outgrowth and branching, which eventually establishes the system of calyces and collecting tubules, ceases at the end of the fifth month. While it is going on, tubules are forming in the metanephrogenic cap (Embryology of the Kidney, p. 1348)

At the time the renal pelvis has acquired its permanent position (in embryos of 9.5 to 13 mm.) the definitive positions of the two poles of the kidney are yet to be established. Subsequently these are pushed cranially or caudally, as the case may be, by the outgrowth of the collecting tubules. In an embryo of 18 mm. Felix found that the cranial pole of the kidney had reached the suprarenal body and was growing forward dorsal to it.

The changes at the caudal end of the ureteral bud are closely related to the developmental changes in the urogenital sinus. As described under Embryology of the Bladder (p. 943), in embryos of 5.3 mm. the cloaca becomes divided, by the downward growth of the urorectal septum, into the dorsal *rectum* and the ventral *primitive urogenital sinus*. At about 11 mm. the primitive urogenital sinus subdivides into two parts: the dorsal *vesico-urethral anlage* and the ventral *pars phallica*. Into the former open the mesonephric ducts. At first the mesonephric ducts open into the latero-dorsal wall of the vesico-urethral anlage, but, with growth, their proximal ends become dilated and, with enlargement of

the bladder, are taken up into the wall of the vesico-urethral segment. During this process of absorption the ureters, which originally opened on the dorsal walls of the mesonephric ducts, acquire separate openings into the bladder anlage, lateral to the orifices of the mesonephric ducts. The lateral walls of the bladder anlage grow more rapidly than its dorso-median (urethral) wall, so that the ureteral orifices are carried cranially and laterally, while the mesonephric ducts (the ejaculatory ducts) retain their original caudad position, opening close together upon Müller's tubercle. This craniolateral displacement of the ureteral orifices is evident in the embryo 13 to 14 mm. long.

B. ANATOMY OF THE URETER

Size and Course. The ureter proper is a thick-walled, narrow, muscular tube varying from 28 to 33 cm. in length. It is directly continuous with the tapering extremity of the renal pelvis, and runs downward and slightly medially beneath the peritoneum, and, entering the pelvic cavity, passes in front of the sacroiliac joint and eventually opens into the fundus of the bladder by passing obliquely through the vesical wall.

The *abdominal part* of the ureter lies beneath the peritoneum, resting upon the psoas muscle, and is crossed by the spermatic (or ovarian) vessels. The right ureter is in close relation to the inferior vena cava, with the iliac arteries above, the sigmoid flexure to the left, and the ilium to the right. The relations of the right ureter are especially important in differential diagnosis, for a number of conditions may arise there which produce symptoms that are frequently attributed to disease of the appendix.

The ureters enter the bony pelvis by crossing the common iliac arteries. At this point the ducts are only about 2 inches apart.

The *pelvic part* of the ureter, in the male, after crossing the bifurcation of the common iliac artery, curves outward and backward and runs downward on the lateral wall of the pelvic cavity in front of the hypogastric artery to a point opposite the ischial spine. Here it curves medially beneath the vas deferens near its ampulla and opposite the seminal vesicle, to run obliquely for about 2 cm. through the wall of the bladder and open by a slit-like orifice into the vesical cavity at the lateral angle of the trigone.

In the female, the pelvic part of the ureter crosses the bifurcation of the common iliac artery and runs downward along the course of the internal iliac artery behind the ovary and tube to the ischial spine, there-

after continuing forward and downward until it reaches the floor of the pelvis. It then runs medially and forward close to the side of the cervix uteri and upper part of the vagina to reach the fundus of the bladder. At about 2.5 cm. below the level of the external os it pierces the vesical wall and enters the cavity of the bladder. As the ureter approaches the cervix it is accompanied for about 2.5 cm. by the uterine artery, which then crosses the ureter and ascends between the layers of the broad ligament.

Anatomical Narrowings. For most of its length the ureter has an average diameter of 0.5 cm. At three points, however, its caliber is considerably narrowed. These normal constrictions occur (1) where it emerges from the kidney pelvis, (2) half-way down, where it crosses the iliac vessels, (3) at its point of entrance into the bladder wall (juxtavesical portion).

Structure. The ureteral wall is composed of three coats.

The *outer, fibrous* coat (tunica adventitia) invests the entire ureter and renal pelvis, and carries the large blood vessels and the nerves, which are extensively ramified so as to form a plexus which reaches a fuller development on the side next the muscle layer.

The *middle, muscular* coat consists of three layers of unstriated fibers: an external longitudinal, a middle circular, and an incomplete internal longitudinal. Near the renal pelvis the muscle fibers form a "braided membrane" running irregularly in all directions (Satani). The isthmus, however, shows a more systematic arrangement, with longitudinal fibers within surrounded by a circular coat. In the neighborhood of the bladder the longitudinal fibers predominate, the circular fibers becoming less and less evident until, in the intramural portion, they disappear entirely. The longitudinal fibers can be traced on the outer side as far as the level of the ureterovesical orifice.

The *mucous coat* is continuous with that of the bladder below, and is transitional in character. It is smooth and thrown into a few longitudinal folds in the collapsed state. The layers of epithelial cells are firmly wedged together. Beneath the epithelium, and separating it from the muscularis, is a dense layer of fibrous tissue containing many elastic fibers.

Lymphoid tissue exists in considerable proportion throughout the three strata composing the wall of the ureter.

Ureterovesical Valve. No definite sphincter can be detected at the vesical opening of the ureter. Certain structures, however, form a

mechanism to prevent a reflux of the bladder content into the ureter. The duct pierces the bladder wall obliquely, and a half inch or more of its lower end is embedded in the bladder muscle. During contraction of the vesical wall, the terminal portion of the ureter is compressed by the muscle fibers, thus preventing the reflux of urine as the intravesical pressure increases.

The peristaltic action of the ureter itself may also help to prevent reflux.

Blood Vessels. The ureter has an abundant, freely anastomosing blood supply from branches from the renal, common iliac, internal spermatic, uterine or hypogastric, and inferior vesical arteries. The larger vessels run in the outer, fibrous coat, where they anastomose freely. From these, branches pierce the muscularis and stroma of the mucosa, where they form a rich network of capillaries.

The veins arise from plexuses in the stroma of the mucosa. They follow the arteries.

Lymphatics. The lymphatics of the ureter accompany the arteries, and are especially numerous in the stroma of the mucosa. The lymphatic distribution is segmental and not continuous. Those from its upper portion drain into the lumbar and preaortic lymph nodes; those from the central portion drain into the iliac nodes; while those from the intrapelvic portion empty into the hypogastric nodes. Like the arteries which they accompany, the lymphatics anastomose very freely.

The Nerves. It is now generally believed that the ureter has an intrinsic neural mechanism, consisting of nerves, plexuses, and innumerable ganglia, by which it functions automatically and initiates and perhaps regulates its own muscular contractions.

Satani (1919) found nerve fibers and ganglionic cells along the entire course of the ureter, from the renal pelvis to the vesical orifice. Most of the nerve tissue was in the outer, fibrous coat, the mucosa, and submucosa. Between the outer, fibrous coat and the muscular layer he found a well-developed network of large nerve fibers, placed parallel to the ureteral axis. Only in the lower part did he find large ganglia. In the middle portion were located the smallest ganglia, for the most part containing few cells or but a single cell.

The main nerve supply of the ureter is the network between the submucosa and the muscularis. In the muscle coat itself nerve elements are usually very scanty. Most of these fibers appear to run obliquely, as if they penetrated the muscle layer to make connection between the two plexuses in the outer, fibrous and inner, mucous coats. The muscle

layer, therefore, while poor in intrinsic innervation, is surrounded by two nerve networks with many ganglia on both its outer and inner sides, which conduct nervous impulses to the muscle tissue.

An earlier investigator, Maier (1881), also found numerous ganglia in the submucosa and muscularis. Hryntschak (1925), on the other hand, denies their existence. In his very extensive investigations in both man and animals he found ganglion cells limited to the adventitia, none whatever being present in the mucosa or muscularis.

Macht (1917), after studying the reaction of the ureter to drugs, concluded that it is innervated by the dorsolumbar or true sympathetic nervous system and also by the sacral autonomic or parasympathetics, and that there are ganglion cells in its walls.

The ureter's extrinsic preganglionic innervation is derived from numerous sources: the renal, spermatic (or ovarian), aortic, hypogastric, and pelvic plexuses.

C. ANOMALIES OF THE URETER

Ureteral anomalies are far more frequent than the average practitioner has believed. Their clinical recognition has become common with increase in the frequency of cystoscopic and roentgenographic study of patients.

Since an anomalous organ is more susceptible to pathological complications than a normal one, a large proportion of ureteral anomalies are discovered during examination for secondary conditions. Obstructive and infective lesions of the upper urinary tract resulting from them are of frequent occurrence, and such anomalies are therefore of surgical importance to the urologist. There are undoubtedly many, however, in whom the congenital malformation produces no symptoms and who go through life unaware of their abnormality.

It is easy to understand why ureteral anomalies are so common when one considers the complex embryological development of the kidney and ureter through the three stages of pronephros, mesonephros, and metanephros; the migration of the kidney from the pelvis to the lumbar region, and its rotation around its longitudinal axis; and the complicated development of the renal vascular system.

Classification of Ureteral Anomalies. Congenital anomalies of the ureter may be divided into four major groups: (1) anomalies in number, (2) anomalies of position, (3) anomalies of form and lumen, (4) anomalies of termination. There is of necessity a certain amount of overlapping, since many cases may properly be placed in more than one category—

for example, double ureters with ectopic openings, or accessory ureters with blind endings. In the following table we have attempted to group under these four heads the various forms of ureteral anomalies that have been reported.

I. Anomalies in number

- a. Congenital single ureter
 1. Draining solitary kidney
 2. Bifid ureter with single orifice, draining both kidneys
- b. Supernumerary ureter from supernumerary kidney
 1. Entering bladder by third orifice
 2. Joining normal ureter, forming Y (unilateral bifid ureter)
 3. With extravescical orifice
- c. Partial duplication of ureter
 1. Unilateral bifid ureter
 - a. Two pelves; ducts join before reaching bladder (Y ureter)
 - b. Single pelvis; single ureter above, dividing near bladder wall and entering by 2 orifices (inverted Y ureter)
 2. Bilateral bifid ureter; 2 pelves in each kidney, single ureteral orifice on each side
 3. Duplicated ureter on one side, bifid on other; 2 pelves in each kidney
 4. Fusion of several ureters into single lumen outside kidney, with or without formation of a pelvis
- d. Complete duplication
 1. Unilateral
 2. Bilateral
 3. Multiple ureters on one or both sides
- e. Double ureter (2 lumina within single outer coat)
- f. Blind-ending accessory ureters
 1. Bifurcation ending blindly
 2. Accessory ureter entering bladder through accessory orifices; ending blindly at cranial end
 3. Accessory ureter ending blindly at both ends

II. Anomalies of position

- a. Both ureters on one side
 1. Draining unilateral double kidney (opposite kidney missing)
 2. Draining unilateral fused kidney
- b. Crossed ureters; kidneys in normal position
- c. Crossed renal ectopia, with normal vesical openings
- d. Abnormal course of ureters
 1. Due to pelvic or mural position of kidney
 2. Ureter from congenital single kidney opening on opposite side of bladder

III. Anomalies of form and lumen

- a. Congenital stricture
- b. Congenital kinks and spiral twists
- c. Congenital valves
- d. Megalo-ureter (congenital dilatation)
- e. Diverticulum
- f. Anomalous length, dependent upon renal ectopia

IV. Anomalies of termination

a. Anomalous intravesical termination

1. Intramural stenosis
2. Termination in intravesical cyst
3. Termination in vesical diverticulum
4. Bifid ureter with separate ureteral orifices (inverted Y ureter)
5. Ureterocele, or cystic dilatation of vesical end of ureter

b. Extravesical termination

1. Solitary ureter terminating extravasically
2. Ectopic ureteral orifices (1 pair of kidneys)
 - a. Single ureter opening extravasically
 - b. Both ureters opening extravasically
3. Ectopic ureteral orifices (double kidneys)
 - a. Unilateral duplication of ureter, with supernumerary ureter opening extravasically
 - b. Unilateral duplication, both ureters opening extravasically
 - c. Bilateral duplication, with 1 ureter opening extravasically
 - d. Bilateral duplication, with supernumerary ureters on both sides opening extravasically

Anomalies in Number. Variation in the number of ureters is by far the most frequent form of ureteral anomaly. Ureteral duplication with double renal pelves occurs more often than all other ureteral anomalies together. In such cases the kidney may be distinctly supernumerary or of the fused type. "Double" pelves may mean merely an elongation of the upper calyx or two distinct functioning pelves. Double pelves may exist in conjunction with a normal ureter or there may be two pelves with wholly distinct ureters. The two pelves are generally placed one above the other. A double kidney is a further extension of the duplication process. It has been variously estimated that from 1 to 4 per cent of all human beings vary in some degree from the normal number of ureters.

Of the several forms of ureteral duplication that have been recorded, unilateral incomplete duplication with double pelves (bifid ureter; Y ureter) is the most common. The ducts unite at some point before

- reaching the bladder, into which they open through a common orifice. Bilateral bifid ureter, while much less frequent, is not rare.

Blind-ending bifurcations are very rare, and are usually confused with ureteral diverticula. Such ureters may produce more or less severe

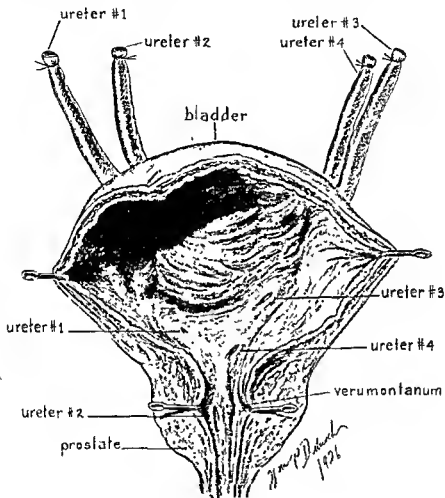


FIG. 275. Bilateral duplication of the ureters. View of the opened bladder and posterior urethra, showing three ureters opening on the trigone and one ureter opening into the prostatic urethra. (Courtesy of Dr. G. S. Huntington, Columbia University Department of Anatomy.)

obstruction, and resection of the offending segment is usually indicated. There may be an accessory ureter opening into the bladder through an accessory ureteral orifice and ending blindly at the cranial end at varying

distances from the bladder. Rarely, a supernumerary ureter will end blindly at both the cranial and caudal ends.

The condition known as ureter bifidus caudalis, or inverted-Y ureter, in which a single ureter starting from the pelvis bifurcates lower down

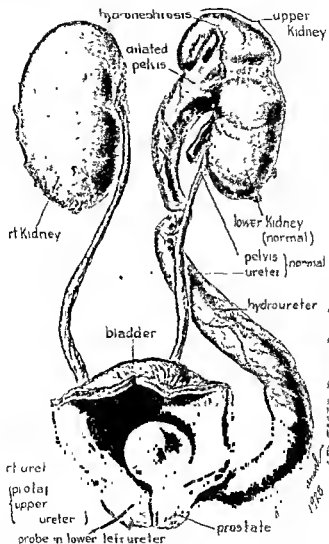


FIG. 276. Unilateral duplication of the ureter. Hydronephrosis, normal ureter and hydro-ureter on the left side; ureterocele. (Christeller.)

and opens through two orifices, one of which may be extravesical, is very rare—less than a dozen cases having been recorded. No satisfactory explanation of the embryology of this condition has been advanced.

Triplication of the ureter and pelvis is of the greatest rarity. In a very interesting case described by Lau and Henline (1931) there was a single ureter and bifid pelvis on the left side and three ureters on the right, one of which led to an aplastic ectopic kidney and two to the upper and lower halves of a double kidney. Cystoscopy showed three ureteral orifices in the right angle of the trigone and one in the left.

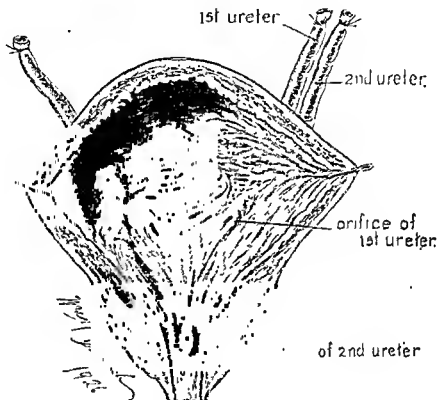


FIG. 277 Unilateral duplication of the ureter. View of opened bladder and posterior urethra, showing the accessory ureter opening on the verumontanum.

Much less common than bifid ureter is duplication of the duct in its entire extent. This, also, may be bilateral or unilateral—more often the latter. The ureters usually leave the pelves at a normal angle. Each duct opens into the bladder through its own orifice, the one above the other; or one ureter may open into the bladder and the other extravasically. The two ureters may run parallel to one another in their entire course, or they may cross each other on their way up. The most

common points of crossing are just above the bladder and below the ureteropelvic juncture. Very rarely the ureters may be partially or entirely enclosed in a common sheath.

In a review of the literature in 1922, Harpster, *et al.* collected 382 cases of ureteral duplication, divided as follows: bilateral complete, 40; unilateral complete, 181; bilateral incomplete, 28; unilateral incomplete, 133. In 144 cases of duplication reported by Braasch and Scholl in 1922, the duplication was divided as follows: bilateral complete, 8; unilateral complete, 36; bilateral incomplete, 1; unilateral incomplete, 99. In a series of 4,215 autopsies reported on by Lowsley, Kingery, and Clarke in 1924, there was unilateral complete duplication of the ureters in 8 instances; bilateral incomplete duplication in 3; and unilateral incomplete duplication in 7. No bilateral complete doubling was observed. Complete absence of a ureter was noted twice.

Anomalies of Position. There is rarely displacement of the ureter except in association with solitary or malformed kidneys, or simple or crossed renal ectopy. In crossed ectopy the cystoscopic appearance of the bladder is normal, but the ureters cross in such a way that the duct from the right kidney enters the bladder on the left side, and vice versa. Aberrant blood vessels may cause more or less abnormality in the position of the ureter (Ureteral Obstruction Due to Aberrant Vessels, p. 1280).

Anomalies of Form and Lumen. Anomalies of form and lumen include congenital (1) strictures, (2) spiral twists and kinks, (3) dilatation, or megalo-ureter, (4) diverticulum.

Congenital strictures usually occur at the points of physiological constriction, that is, at the ureteropelvic junction, about the center of the ureter's extent at a point where it comes in contact with the iliac vessels, and in its juxtavesical portion. They are found mostly in the fetus and newborn and at autopsy. Intramural stenosis is referred to below in connection with anomalies of termination.

Spiral twists and kinks are sometimes undoubtedly of congenital origin. Kinks are usually found in connection with faulty modes of origin of the ureter from the renal pelvis, but they may also occur at a number of different levels, doubtless resulting either from abnormal motility of the kidney or from excessive length of the ureter itself. A kink or angulation may also be secondary to an aberrant blood vessel interfering with the normal course of the ureter.

Megalo-ureter, or congenital dilatation of the ureter, is a condition in which there is permanent gaping of the ureterovesical orifice with a greatly dilated ureter. The condition is frequently bilateral.

Diverticulum of the ureter is very rare, and may be either congenital or acquired. It may readily be confused with a ureteral bifurcation with a blind ending, and some of the cases reported in the literature are really bifurcations.

Each of these various abnormalities of form and caliber of the ureter may be either congenital or acquired. Both forms—the congenital and the acquired—will be considered together in the following chapter devoted to Injuries and Diseases of the Ureter (Stricture, p. 1270; Kinks and Angulations, p. 1277; Megalo-ureter, or Dilatation of the Ureter, p. 1291; Diverticulum, p. 1257).

Anomalies of Termination. *Intramural stenosis* is occasionally encountered in the newborn. In an adult, this condition cannot be differentiated from an acquired stricture (Stricture of the Ureter, p. 1270).

Ureterocele, or cystic dilatation of the vesical end of the ureter, is sometimes congenital, but in other cases it is undoubtedly an acquired condition. Differentiation between the congenital and acquired types may be extremely difficult or impossible (Ureterocele, p. 1285).

Ectopic ureteral endings are not uncommon, and probably occur about equally in both sexes. In the female, they usually produce incontinence and are therefore discovered; but in the male, they cause fewer symptoms and are frequently overlooked. Sometimes one or both otherwise normal ureters terminate extravasically. Again, the normal ureters will terminate in their proper places in the bladder, but supernumerary ones will end extravasically. In the male, the ectopic opening is into the prostatic urethra, a Cowper's gland, seminal vesicle, ejaculatory duct, or vas deferens. These are all of mesonephric-duct origin. In the female, the opening is into the urethra, vestibule of the vagina, vagina, tube, or uterus. In either sex, the ureter may terminate in the rectum, vesical neck, or some portion of the bladder other than the normal site.

In the largest group of cases collected to date, that of Thom (1928), 63 of the 185 patients were males, 117 females, and in 5 cases the sex was not mentioned. The cases were divided as follows:

Single ureter with extravasical orifice	58
Bilateral single ureter with extravasical orifice.....	6
Unilateral duplication with extravasical opening of accessory ureter....	96
Complete ureteral duplication on 1 side with extravasical opening of both ureters	2
Bilateral complete duplication with extravasical opening of only 1 ureter....	21
Bilateral ureteral duplication with extravasical opening of all 4 ureters	2

In the male, the opening was found into the prostatic urethra, 33 times; seminal vesicles, 17 times; vasa deferentia, 6 times; ejaculatory ducts, 5 times. In the female, the opening was into the urethra, 37 times; vestibule, 45 times; vagina, 32 times; uterus, 3 times.

In a case reported by Lowsley and Conroy, there was a double kidney on the left side with double ureter, the accessory ureter opening into the vaginal vestibule. The 23-year-old patient had had continual leakage of urine since birth, and had been told that she had a vesicovaginal fistula. Vaginal examination showed, 1 cm. below the urethra and to the left of the midline, a small opening, which emitted spurts of clear fluid. A probe inserted into this opening passed easily into what was thought to be the bladder, giving the impression that this was a vesicovaginal fistula. The probe was withdrawn, and a ureteral catheter was inserted for 20 cm. Cystoscopy, however, revealed no evidence of the catheter. Both ureteral orifices appeared normal in size and location. It was decided that the patient had an accessory ureter opening into the vaginal vestibule. Retrograde pyelography confirmed this and showed a double left kidney. The accessory ureter, leading to the upper kidney, was greatly dilated due to a stricture at its lower end. The ureter from the lower kidney was normal. The accessory left kidney, with a portion of its dilated aberrant ureter, was removed under rib-resection technic. The patient was discharged 23 days later, with the wound healed and her incontinence cured.

Etiology of Ureteral Anomalies. To understand how ureteral duplication may occur it is necessary to review the earliest development of the ureter. At about the fourth week of embryonic life the anlage of the ureter, renal pelvis, and calyces makes its appearance as a hudding from the mesonephric duct close to the point where it enters the cloaca (*Embryology of the Ureter*, p. 1208). The ureteral bud grows first dorsally and then cranially. Its blind end becomes dilated, forming the primitive renal pelvis. A cap of metanephrogenic tissue covers the dilated end. Subsequently the dilated blind end divides into a cephalic and a caudal branch and two or more smaller central evaginations, which become the calyces and straight tubules of the adult kidney.

It is readily seen that the various degrees of duplication of the ureter and renal pelvis may occur as the result of premature or exaggerated splitting of the ureteral bud, so that the split is not confined to the tip alone but extends for some distance downward along the ureteral stalk. Most embryologists attribute complete duplication to the giving off of

two or even more ureteral buds from the mesonephric duct. The great majority of congenital anomalies of the ureter are dependent upon changes in the normal development of the ureteral bud, and are therefore in existence by the third month of fetal life.

Since, in the preponderance of embryological material, the ureteral buds are seen to grow dorsally, keeping close together and carrying their caps of mesodermic cells upward, it is logical to assume that variations from this course might produce certain of the anomalous formations observed in clinical practice. Should the ureteral buds lie closer together than normally, there might result one of the numerous forms of fused kidney, with displacement of the ureters. Even in fused kidneys, however, the course and termination of the ureters may be entirely normal, though there is almost always some variation in their length.

The question of the origin of the various types of ureteral duplication is by no means clear, and none of the explanations thus far advanced satisfactorily accounts for all forms.

Practically nothing is known regarding the origin of congenital strictures, kinks, and angulations. *Spirality* is a marked characteristic of any duct arising from the wolffian body (ureter, oviduct, uriniferous tubules). Evidences of the original spirality of the ureter are often seen at autopsy. Thus, the occurrence of congenital kinks or angulations might easily be explained.

There is a similar paucity of authentic data concerning the origin of congenital dilatation of the ureter. It has been demonstrated that in the embryo the ureter is of relatively greater size than in the adult. Persistence of this condition would account for the widely dilated ureters occasionally seen for which no pathological cause is evident. Again, it may well be that congenital dilatation is not an anomaly *per se*, but dependent upon some other malformation in the urinary tract.

Symptoms of Ureteral Anomalies. Pathological complications are much more likely to occur in congenitally malformed kidneys and ureters than in normal organs. Mertz (1920), in a review of 300 cases, found pathological complications in 30 per cent; while Hawthorne (1936), in a report of 63 cases of duplication, found hydronephrosis in 48 and infection in 50. Since duplicated ureters and kidneys give no symptoms unless attacked by disease, it is usually when the patient seeks treatment of these secondary conditions that the anomaly is discovered. Clinically, the various pathological conditions found in duplicated kidneys and ureters are essentially the same as when they occur in the single

kidney. We have found infection to be the most common complication, with hydronephrosis second in frequency, and stone third. These sequelae are the result of stasis, which is frequent in the course of ureteral anomalies, due to irregular peristalsis, twisting and kinking of one ureter about the other, anomalous insertion into the bladder, etc. In most cases of unilateral abnormality observed by us the opposite side was healthy.

Where congenital twists, kinks, and dilatations exist, symptoms referable to the urinary tract appear very early. It is probable that many subjects of these malformations die so early that the anomaly is not searched for, or even suspected. The thorough scrutiny of the urinary tract which is necessary to demonstrate such conditions would hardly be undertaken unless some very pronounced urinary symptoms were present. The symptoms and diagnosis of congenital anomalies of form and lumen will be considered more fully later on, in connection with acquired abnormalities of a similar nature.

Ureteral ectopies in females as a rule open below the sphincter, so that constant dribbling early brings them under urological examination. This probably explains, in part at least, the large proportion of females among the reported cases. The common use of cystoscopy and pyelography has resulted in many unexplained cases of incontinence in women being traced to such ectopic openings. In men, the ectopic orifices are likely to be located within sphincteric control, and, no incontinence existing to call attention to them, they are only discovered accidentally, when secondary infection, stone, or back pressure may produce symptoms leading to an examination. Persistent disturbances of urination or pyuria in either a child or an adult require a thorough urological examination, bearing in mind the possibility of ureteral ectopies.

Diagnosis. The routine use of retrograde and intravenous pyelography has proved of great value in the early clinical recognition of ureteral anomalies.

Under normal conditions, *complete duplication* of the ureter and pelvis can usually be recognized with relative ease by cystoscopic inspection, and the diagnosis confirmed by the use of x-ray catheters and ureteropyelograms. The ureteral orifices are usually situated close together and at approximately the normal location in the lateral portion of the trigone. At times, however, they are widely separated and placed in abnormal parts of the bladder, so that their discovery may be very difficult. When the bladder is acutely inflamed, multiple orifices may

easily be overlooked. One should always bear in mind the possibility of duplicated ureters during routine cystoscopy, and make a careful search for accessory orifices. Catheters may be passed into each of the ureteral orifices, specimens obtained for the usual examinations, and functional tests performed for the estimation of the function of the separate segments of the double kidney.

The diagnosis of *incomplete duplication* occurring above the bladder, the most common anomaly, is dependent upon the routine use of pyelo-ureterography. The presence of pathological complications in one or both segments of a bifid ureter may render the recognition of the anomaly very difficult. The duplicated ureter may become occluded so that the pyelo-ureterogram does not show the duplication. When performing retrograde pyelography, it will be found advantageous to raise the patient to an upright position during the final exposure, withdraw the catheters until the tips are about 2 cm. from the ureteral orifices, and inject a little more of the opaque solution. This serves to give greater clarity to the outline, and often reveals bifid ureters which would not be discovered were the contrast medium injected in the customary way. Correct interpretation of the roentgenograms thus obtained requires considerable study and practice.

Not only should the separate segments of a double kidney be studied as to function and the presence or absence of pathological changes, but it is of practical importance to ascertain, by urography, the relative size of the two pelves, the distance separating them, and whether or not they communicate, as these factors have important bearings upon the treatment.

Congenital strictures, twists, dilatations, and diverticula are well demonstrated on the pyelo-ureterograms, and are readily detected on routine pyelo-ureterography, although differentiation between congenital and acquired forms may be impossible. The symptoms of stricture due to *aberrant vessels* are by no means characteristic, as a long list of unavailing appendectomies bears witness. In view of the relatively frequent occurrence of aberrant vessels and otherwise anomalous ureters, every clinician should keep in mind the possibility of their existence and insist on a search being made for them before radical measures are undertaken. Undoubtedly, many unnecessary operations would thus be avoided.

If the ureteral catheter is arrested or the renal pelvis reached sooner than normally it should be, renal dystopia should be thought of, though

its actual demonstration is dependent upon roentgenography. Crossed renal ectopy gives no hint of its existence cystoscopically, since the ureteral orifices are normal in appearance and position.

Ectopic openings into the urethra or vagina may be difficult to locate, but their discovery is facilitated by the intravenous administration of indigo-carmin. With modern urethrosopes one can frequently locate and catheterize the ectopic orifice when in the urethra. In every case of unexplained incontinence or persistent pyuria a careful search should be made for ectopic openings.

Cystoscopy, by revealing abnormality in the number of the ureteral orifices, is of value. For example, if no orifice is seen, there may be one kidney with an ectopic ureter or two kidneys, both of which end extravasically. If only one orifice is found in the bladder, it may indicate absence of one kidney and ureter or the presence of a normal ureter on one side with an ectopic ureter on the other. It must be borne in mind that if two orifices are seen in the normal position in the bladder, there may be one or two accessory ureters draining extravasically. Occasionally, a dilated accessory ureter passing under the bladder mucosa can be observed cystoscopically.

Intravenous urograms are of value in diagnosing extravasical orifices and ureteral duplications provided there is sufficient functioning tissue in the renal mass belonging to the ectopic ureter to eliminate the contrast medium.

After an ectopic opening has been located, its relation can be shown by retrograde or intravenous pyelography. It is important not only to make the diagnosis of ectopic ureter and to locate the extravasical opening, but also to ascertain the condition and function of the kidney drained by the ectopic ureter. If the ectopic ureter is an accessory duct, one should learn not only the condition of the portion of the kidney drained by it, but also the condition of the other part of the kidney. Full information regarding the kidney on the other side is, of course, essential.

Prognosis. The outlook as a rule depends on the prognosis of the secondary pathological condition which led to discovery of the ureteral anomaly.

Treatment. Duplication in itself is symptomless, and requires no special form of treatment. A ureteral anomaly which is discovered accidentally and is unaccompanied by pathological complications is usually best left undisturbed. In the more common cases presenting

secondary pathological conditions, the treatment is that required for the complication present. Hydronephrosis, infection, and stone are the most common complications. It should be borne in mind, when treating adult patients whose anomalous ureters have only recently caused them difficulty, that such deformities will probably be amenable to treatment similar to that applicable when anatomically normal organs have become diseased. If only a pyelitis is present, conservative treatment may suffice. A considerable percentage of these cases, however, eventually require operation. Surgery should be conservative whenever possible. Many surgeons get rid of a troublesome abnormal ureter by removing a functioning kidney—a doubtful procedure in our opinion, unless there is marked disease of the entire kidney with a competent kidney on the opposite side. Plastic operations solve many of these problems. Re-implantation of a misplaced and poorly functioning ureter has restored many urinary mechanisms to normal capacity. Heminephrectomy is applicable in many cases with double or supernumerary kidneys and ureters. A supernumerary ureter, especially if its opening be extravesimal, may sometimes be removed without injury to the kidney proper, or its proximal end may be reimplanted into the bladder.

The surgical treatment of ureteral anomalies is considered under Surgical Treatment of the Ureter (p. 1302).

D. PHYSIOLOGY OF THE URETER

The function of the ureter is the transportation of the urine from the renal pelvis to the bladder. If the transportation system is disorganized by some interference with ureteral function, such as that resulting from stricture, impacted stone, or new growth, the kidney will be seriously affected or even completely destroyed. If the disturbance is unilateral, the bladder may continue to function normally, but as a rule the bladder also shares in the general disorganization which even a trifling lesion of the ureter is capable of producing. The great importance of this duct, and its influence upon the rest of the urinary tract, thus becomes evident.

Ureteral Peristalsis. The urine is propelled from the renal pelvis to the bladder by rhythmical peristaltic contractions which travel at a rate of 1 to 5 a minute in man, depending upon the volume of urine secreted by the kidney. The urine therefore reaches the bladder not in a continuous stream but in spurts.

The normal peristaltic movements of the ureter were studied by Lucas (1904), who found that a suction followed the peristaltic wave,

while at the same time a force was exerted on the fluid in front of the wave. In the normal ureter the pressure remains low in the renal pelvis because of an anatomical arrangement which prevents the pelvis from collapsing under negative pressure, that is, there exists a rhythmic movement of the pelvis which has a "milking action" upon that portion of the pyramid which projects into it. An increased flow of urine calls forth a brisker peristalsis and therefore does not produce an increase of pressure. Lucas noted that in the vesical end of the ureter contractions are smaller but occur oftener than in the middle section. It is reasonable to suppose that these contractions have some influence in preventing regurgitation.

The rate of the ureteral peristaltic waves varies according to the extent of the kidney's activity. The extent of the waves is also subject to considerable variation. Sometimes they run from one end of the ureter to the other; again they may be observed to originate at the renal pelvis, but die away before the bladder wall is approached. Small local waves can also be seen, being visible only in a restricted area in any segment of the ureter.

During the last decade some very definite additions to our knowledge of ureteral peristalsis and physiology have been made by H. R. Trattner (1932), who studied the function of the human ureter by the aid of the "hydrophorograph" (water-wave recorder). He found that ureteral peristalsis consists of (a) a longitudinal contraction which shortens the ureter and narrows but does not obliterate its lumen, and (b) a circular contraction which momentarily obliterates the lumen in successive segments of the ureter as the wave advances. The tonus of the ureteral musculature and the strength of contraction determine the degree of shortening and narrowing of the ureter by the longitudinal contraction and the degree of encroachment on the lumen by the circular contraction. The longitudinal and circular fibers contract almost simultaneously, but the longitudinal wave quickly involves the entire duct. The circular wave can be seen coursing successive segments of the ureter while the duct remains longitudinally contracted; when the circular wave ceases, complete relaxation occurs. *During relaxation, pendulum-like movements of the longitudinal muscle may appear; these are not concerned with the propulsion of urine.* Trattner observed that peristalsis may begin in the middle or lower third of the ureter, this being frequently followed by peristalsis of the entire duct.

Factors that Influence Ureteral Peristalsis. Many factors have been

demonstrated to influence ureteral peristalsis: age, sex, blood flow and oxygen-carbon-dioxide content of the blood, nutrition, diuresis, the concentration of the urine, intra-abdominal and intravesical pressure, inflammation, bacterial toxins, and the intraureteral or systemic administration of certain drugs.

Ockerblad and his co-workers found that when morphine was given subcutaneously in the usual clinical doses, ureteral tone, as well as the extent of the ureteral contractions, was greatly increased. Atropine, in doses of one one-hundredth of a grain, invariably wiped out the contractions which morphine had stimulated in the urine, resulting in decided loss of tone; but atropine used alone produced no noticeable effect on muscle tone. These experiments indicate that the usual conception of a quieting effect upon the ureter, obtained by the administration of morphine, is incorrect. Actually, morphine stimulates but never acts as a sedative to the ureteral muscles.

Ureteral Antiperistalsis. Until quite recently it was believed that reverse peristalsis never took place in the ureter. Trattner, however, observed that while both longitudinal and circular contractions usually begin at the upper end of the ureter and proceed toward the bladder, both waves may also originate at the vesical end and travel toward the kidney. Waring exhibited a calculus formed about a piece of grass which the patient admitted having introduced into his urethra more than a year earlier. This calculus was found in the right renal pelvis, and the only explanation of its presence there seemed to be that it had been carried up the ureter by reverse peristalsis. Braasch reported the finding of a hairpin calculus embedded in the right ureter.

Vesico-ureteral Reflux. Investigators differ in their opinions as to whether or not it is possible for vesico-ureteral reflux to occur under normal conditions. It is well known that regurgitation of urine can occur under conditions of disease or dysfunction of the bladder or ureter, resulting in loss of muscle tone and alterations in the ureterovesical valve—the simple mechanical contrivance which normally prevents reflux. Such pathological conditions include back pressure due to prostatism or valves of the posterior urethra, infections of the bladder, stone, etc. Primary atony of the ureter and complete congenital dilatation may produce like results. Although vesico-ureteral reflux is much more frequent in pathological than in normal conditions, it has been cystographically demonstrated in normal persons, both children and adults, in numerous instances.

The entire question has been elaborately studied by Graves and Davidoff, who concluded that the phenomenon of reflux exists but depends primarily upon sustention of the bladder tonus as the muscle actively resists distention. If such a pathological condition as obstruction of the vesical neck is present, none of the mechanism which normally prevents the bladder content from regurgitating up the ureters is sufficiently efficient when the bladder contracts vigorously.

BIBLIOGRAPHY

- ANSON, B. J., AND RIBA, L. W.: Anatomical and surgical features of ectopic kidney. *Surg. Gynec. Obst.*, 68: 37, January 1939.
- BAILEY, F. R., AND MILLER, A. M.: Text-book of embryology. Ed. 2. N.Y., William Wood & Co., 1911.
- BAINES, G. H.: Supernumerary and ectopic ureters. *Brit J Surg*, 28: 314, 1940.
- BARCLAY, I. B., AND BAIRD, J. B.: Incidence of congenital abnormalities of the genito-urinary tract as seen in 500 consecutive intravenous pyelographies. *Lancet*, 2: 1169, 1935.
- BARRINGER, B. S.: Observations on the physiology and pathology of ureteral function. *Folia Urologica*, 2: 463, 1903.
- BEER, E., AND FERBER, W. L. F.: Crossed renal ectopia. *J. Urol.*, 33: 541, 1937.
- BRAASCH, W. F.: Urography. P 439 *et seq.*, Phila. W. B. Saunders Co., 1928.
- BRAASCH, W. F., AND SCHOLL, A. J.: Pathologic complications with duplication of the renal pelvis and ureter (double kidney). *J. Urol.*, 8: 507, 1922.
- CAMPBELL, M. F.: Surgical treatment of anomalies of the upper urinary tract in children. *J. A. M. A.*, 116: 193, 1936.
- CAMPBELL, M. F.: Ectopic ureteral orifice; 17 cases in children. *Surg., Gynec. & Obst.*, 64: 22, 1937.
- CAULE, J. R.: Megalo-ureter; the importance of the ureterovesical valve. *J. Urol.*, 9: 315, 1923.
- CRENSHAW, J. L.: Ureter with extravescical orifice, etc. *J. Urol.*, 43: 82, 1940.
- DELMAS, J., AND DELMAS, P.: Sur les anomalies urétérales. *Ann. d. mal. d. org. Génito-Urin.*, 1: pp. 769, 865 and 984, 1910.
- DRAPER, J. W., 2ND, AND BRAASCH, W. F.: The function of the uretero-vesical valve. *Trans. A. M. A. Sect. Genito-Urin. Dis.*, June 1912.
- EISENDRATH, D. N.: Congenital strictures and spiral twists of the ureters. *Ann. Surg.*, 65: 552, 1917.
- EISENDRATH, D. N.: Ureteral strictures, kinks and abnormal inserts. *Surg. Gynec. Obst.*, 41: 557, 1925.
- EVERETT, H. S.: Ureteral ectopia; report of case, with discussion of treatment. *Southern M. J.*, 31: 843, 1938.
- FELIX, W.: The development of the urinogenital organs. Keibel and Mall: *Manual of human embryology*. Vol. 2, Chpt. 19. Phila., J. B. Lippincott Co., 1912.
- FREEMAN, I.: Urethral ectopic ureter in female, without incontinence; case (with bilateral ureteral and pelvic reduplication). *J. Urol.*, 39: 393, 1938.
- FURNISS, H. D.: Supernumerary ureters with extravescical openings. *J. Urol.*, 37: 341, 1937.
- GRAVES, R. C., AND DAVIDOFF, L. M.: Studies on the ureter and bladder, with special reference to regurgitation of the vesical contents. *Trans. Am. Assoc. Genito-Urin. Surg.*, 16: 25, 1923.

- GRUBER, C. M.: Effect of morphine and papaverine upon the peristaltic and antiperistaltic contractions of the ureter. *J. Pharmacol. & Exper. Therap.*, 33: 191, 1928.
- GUTIERREZ, R.: Role of anomalies of kidney and ureter in causation of surgical conditions. *J. A. M. A.*, 106: 183, 1936.
- HARPSTER, C. M., BROWN, T. H., AND DELCHER, H. A.: Abnormalities of the kidney and ureter. *J. Urol.*, 8: 459, 1922.
- HARRIS, AUGUSTUS: Ureteral anomalies, with special reference to partial duplication with one branch ending blindly: 2 cases with renal obstruction cured by surgical resection. *J. Urol.*, 38: 442, 1937.
- HAWTHORNE, ALLAN B.: Embryologic and clinical aspects of double ureter. *J. A. M. A.*, 106: 3, 1936.
- HENDERSON, V. E.: The factors of ureter pressure. *J. Physiol.*, 33: 175, 1905.
- HEPBURN, T. N.: Kidney-ureter anomalies. *Ann. Surg.*, 48: 294, 1918.
- HEPBURN, T. N.: Observations on the ureterovesical valve. *Surg. Gynec. & Obst.*, 36: 368, 1928.
- HEPBURN, T. N.: Extravesical opening (from rudimentary double left kidney) causing urinary incontinence. *Ann. Surg.*, 98: 110, 1933.
- HRYNDSCHAK, T.: Zur anatomie und physiologie des nervenapparates der harnblase und des ureters. Separatabdruck aus arbeiten aus dem Neurologischen Institut an der Wiener Univ., 24: 2 and 3, Franz Deuticke, Wien., 1923.
- HRYNDSCHAK, T.: Beiträge zur physiologie des ureters I. Zur harnleiterautomatie. Sonderabdruck aus Pflüger's Arch. f. d. gesam. Physiol. des Menschen und der Tiere, 209, 4: 542-561, Berlin, Julius Springer, 1925.
- HRYNDSCHAK, T.: Zur anatomie und physiologie des nervenapparates der harnblase und des ureters II. Mitteilung Über den ganglienzellapparat von nierenbecken und harnleiter des menschen und einiger saugetierte. *Ztschr. f. Urolog. Chir.*, 18: 1/2, 86-110, Berlin, Julius Springer, 1925.
- JORDAN, H. E., AND KINDRED, J. E.: *A Textbook of Embryology*. N. Y., D Appleton & Co., 1926.
- KEITH, ARTHUR: *Human Embryology and Morphology*. Ed. 4. London, Edward Arnold, 1921.
- KILBANE, E. F.: Ectopic ureteral openings. *Surg. Gynec. & Obst.*, 42: 32, 1926.
- KIRWIN, T. J.: The role of the ureter in diseases of the genito-urinary tract. *Am. J. Surg.*, 4: 355, 1928.
- KIRWIN, T. J.: Clinical value of experimental ureteral implantation. *Am. J. Surg.*, 23: 14, 1934.
- KRETSCHMER, H. L., AND GREER, J. R.: Insufficiency at the uretero-vesical junction. *Surg. Gynec. Obst.*, 21: 228, 1915.
- LATARJET, A., AND BERTRAND, P.: Recherches anatomiques sur l'innervation des capsules surrénales, des reins et de la partie supérieure de l'urètre. *Leçons Chirurgicales*, 20: 452, 1923.
- LAU, F. T., AND HENLINE, R. B.: Ureteral anomalies. report of case manifesting 3 ureters on one side with 1 ending blindly in an aplastic kidney and a bifid pelvis with a single ureter on the other side. *J. A. M. A.*, 96: 587, 1931.
- LEGUEU, F., AND PAPIN, E.: De la dilatation permanente des orifices urétéraux et du reflex vesico-renal. *Arch. Urol. de la Clin. Necker*, 1: 377, 1913.
- LOWSLEY, O. S., AND CONROY, FRANK.: Aberrant ureter and its treatment: report of case. *J. Urol.*, 48: 611, 1942.
- LOWSLEY, O. S., KINGERY, L. B., AND CLARKE, H. C.: The surgical significance of certain abnormalities of the urinary tract. *J. Urol.*, 2: 293, 1924.

- LUCAS, D. R.: *On intraureteral pressure and its relations to the peristaltic movements of the ureter.* Proc. Soc. Exper. Biol. & Med., 2: 61, 1904-5.
- LUCAS, D. R.: *On the abnormal peristaltic movements of the ureter.* Proc. Soc. Exper. Biol. & Med., 4: 6, 1906
- MACHT, D.: *A contribution to the physiology of the ureter and vas deferens* J. Urol., 1: 97, 1917.
- MAIER, R.: *Die ganglien in den harnabführenden wegen des menschen und einiger tiere* Virchow's Arch. f. path. Anat., 85: 49, 1881.
- MERTZ, H. O.: *Bilateral duplication of the ureters, with a compilation of recorded cases* Urol. & Cutan. Rev., 24: 636, 1920.
- MERTZ, H. O., AND HAMER, H. G.: *Importance of anomalies in diagnosis and treatment of diseases of the urinary organs.* J. Indiana Med. Assoc., 17: 239, 1924.
- OCKERBLAD, N. F., CARLSON, H. E., AND SIMON, J. F.: *Effect of morphine upon the human ureter.* J. Urol., 33: 356, 362, 1935. Also: Southern M. J., 29: 166, 1936.
- OTTOW, B.: *Kyste du vagin et dédoublement des urétéres.* J. d'Urol., 46: 577, December 1938.
- PAPIN, L., AND EISENDRATH, D. N.: *Classification of renal and ureteral anomalies.* Ann. Surg., 85: 755, 1927.
- PAULUS, G.: *Enuresis due to double ureter: clinical aspects.* Zentralbl. f. Gynäk., 65: 1136, 1941.
- POHLMAN, A. G.: *A note on the developmental relations of the kidney and ureter in human embryos.* Johns Hopkins Hosp. Bull., 16: 49, 1905.
- POHLMAN, A. G.: *Abnormalities in the form of the ureter and kidney dependent on the development of the renal bud* Johns Hopkins Hosp. Bull., 16: 167, 1914.
- QUINBY, W. C.: *Observations on the physiology and pathology of the ureter* J. Urol., 7: 259, 1922.
- ROBINSON, B.: *Remarks on ureteral anomalies* Texas Med. News, 13: 372, 1903-4.
- SACQUEPEE, E.: *Urétère double et urétère bifide chez homme.* J. de l'anat., 36: 103, 1900.
- SATANI, Y.: *Histologic study of the ureter.* J. Urol., 3: 247, 1919.
- SATANI, Y.: *Experimental studies of the ureter.* Am. J. Physiol., 49: 474, 1919.
- SOLOWAY, H. M.: *Bilateral and unilateral renal agenesis.* Ann. Surg., 109: 267, February 1939.
- TROM, B.: *Surgical treatment of double ureters and double kidneys and of ureters opening extravasically.* Ztschr. f. Urol., 22: 417-468, 1928.
- TRATTNER, H. R.: *Graphic registration of the function of the human ureter with the hydrophorograph. Considerations in physiology and pathologic physiology of the ureter.* J. Urol., 28: 1, 1932
- WARING, T. P.: *Can solid material by reflux or antiperistalsis enter the pelvis of the kidney from the bladder? A case proving that it can.* Trans. Southern Surg. Assoc., 41: 346, 1928.
- WHARTON, L. R.: *The innervation of the ureter, with respect to denervation.* J. Urol., 28: 639, 1932
- WISLOCKI, G. B., AND O'CONOR, V. J.: *Experimental observations upon the ureters, with special reference to peristalsis and antiperistalsis* Johns Hopkins Hosp. Bull., 31: 197, 1920
- WU, P. P. T.: *Relative activity of the various portions of the excised ureter of the dog* J. Urol., 30: 307, 1933



CHAPTER XXXIV

INJURIES AND DISEASES OF THE URETER

A. INJURIES TO THE URETER

Etiology and Pathology. *Traumatic Injuries.* The ureter is seldom subject to traumatic injury. Occasionally, in cases of extraordinary violence, such as automobile or industrial crushing accidents, the duct may be traumatized. Ordinarily, however, its mobility and small size protect it from trauma, even though the kidney or bladder may be injured.

Ureteral trauma may take one of several forms. The duct may be punctured by slivers of bone, glass, or metal; it may be pierced by revolver bullets or bits of shrapnel; it may be torn, partially or completely, into two fragments; it may be slit, leaving a clean cut, which heals readily by first intention; or it may have a gaping wound gouged from its wall, with ragged edges which quickly invite infection and cannot be drawn together because of too great loss of substance. Wounds inflicted by missiles from firearms are even more uncommon than those incurred in traffic or industrial accidents. Up to 1931 only 7 such cases had been reported in medical literature (Le Comte), and even in war-time, gunshot injuries to the ureter appear to be very rare.

Injuries Incurred During Ureteral Instrumentation. Puncture of the ureter during catheterization occasionally occurs. This is much more likely to happen if the wall has been weakened by disease. This possibility of rupture or penetration during diagnostic or therapeutic maneuvers sometimes assumes medico-legal importance. Wesson collected a number of such cases from the literature and from his own clinical experience and that of some of his colleagues. Examination of the case records revealed that in every case the ureter under investigation was diseased before the instrument was introduced. From experiments upon cadavers, Wesson concluded that the wall of a normal ureter cannot be punctured by the usual ureteral catheter, and it is doubtful if a diseased ureter can be perforated unless a deep ulcer is present.

There is always a possibility that rupture of the ureter may have occurred before exploration was attempted, but this not having been

recognized, the damage to the wall is assumed to be the result of the instrumentation. A few cases have been reported of stones eroding through all the coats of the ureteral wall.

Henline, in 1934, reported 9 cases of instrumental trauma to the ureter occurring in our service and briefly reviewed the literature. It was his opinion that accidental injuries to the ureter during diagnostic exploration or the introduction of instruments for therapeutic purposes is a more frequent occurrence than the reports in literature would indicate. It should be impressed upon the mind of every practitioner that while a normal ureter is not readily traumatized by the ordinary ureteral catheter, a diseased ureter may be highly friable in more or less of its extent and easily injured. Instrumental manipulation in a diseased ureter must be carried out with the utmost caution; and in such circumstances as the removal of a ureteral stone, the relative merits of intraureteral manipulation, and removal through an external surgical incision which can be controlled and properly repaired, should be carefully weighed.

Surgical Injuries. Injury to the ureter is most likely to occur during the course of extensive surgical interventions, especially gynecological operations, such as the removal of large uterine fibroids which may have displaced the ureter from its normal position. Such a mishap may also take place during the removal of diseased fallopian tubes, intraligamentous cysts, uterine carcinomas, and tumors of the bladder, or in the course of a difficult instrumental delivery, an extrauterine pregnancy, or a seminal vesiculectomy. It is probable that unintentional severing or ligation of one or both ureters not infrequently goes unrecognized, and that many postoperative deaths attributed to other causes may be traceable to this accident. "Injuries to the ureter are by no means uncommon accidents, even though few of them ever find their way into print," remarked Baldy in 1896; and this statement probably still holds true.

Neither do hospital services show the actual incidence of operative injuries to the ureter. Stevens, for example, notes that in his own service at the Stanford University School of Medicine only 5 cases of ureteral trauma were noted in 27,708 admissions, and of the 1,086 pelvic operations performed, accidental injury to the ureter was noted but 4 times. To these meager figures he opposes those gleaned from literature by Bland, who collected 310 instances, and by Herman, who found that the ureters had been injured in 86, or about 4 per cent, of a series of 2,225 pelvic operations

Surgical injuries to the ureter are *most likely* to occur (1) in the region of the broad ligament, where it is likely to be included in a ligature of the uterine artery, or (2) in its upper third, in the region of the utero-ovarian pedicle.

The usual types of surgical injury are ligation, incision, resection, clamping, and extensive stripping and interference with the blood supply.

Accidental ligation may be done on one or both sides. The affected ureter is usually completely occluded. Bilateral ligation, of course, produces complete anuria, and unless promptly relieved, the outcome is fatal. Occasionally, a ureter is ligated only partially, causing a stricture or a fistula. The duct may be eroded by a ligature placed too close to its wall, or by closure of the operative wound in such a way that tension is exerted upon the ureter's peritoneal envelop.

An accidental incision of the ureter may be either longitudinal or transverse. A longitudinal cut tends to close spontaneously and is unlikely to produce a stricture when healing. If the cut is transverse, but involves only a portion of the wall, the remaining bridge of tissue will prevent retraction of the two ends and preserve the ureter's continuity, so that it may be possible to pass a catheter from the lower to the upper fragment. If the transverse cut is complete, or if a portion of the ureter is resected, satisfactory repair will be much more difficult.

The ureter may be crushed and bruised by the application of forceps, hemostats, or clamps. Still another injury which it may suffer during pelvic surgery is the extensive stripping off of its adventitia, with severe damage to its vascularization. Both clamping and extensive injury to the blood vessels almost invariably result in necrosis, which will usually be in evidence from 1 to 3 weeks after operation.

Any breach of the ureter's continuity, whether it be caused by primary cutting or by loss of substance through necrosis, usually eventuates in a fistula, which may open into the vagina or cervix; or, rarely, the fistulous tract may lead to the cutaneous surface through the laparotomy wound. Sometimes the entire urinary output of the affected side will be excreted through such a fistula, but more frequently part of the urine will drain into the bladder while a smaller quantity seeps through the fistulous opening into the vaginal canal, producing a greater or less degree of urinary incontinence, depending upon the extent of the ureteral damage. Such a fistula tends to undergo cicatricial contraction, causing more or less complete stricture of the ureter, which will produce ureteral dilatation above and eventually set up a hydronephrotic condition in the kidney of the corresponding side.

David Feiner (1938), reporting 8 cases of operative injury to the ureter and reviewing 253 others reported in previous publications, found the types of injuries represented to be as follows:

Unilateral Injury to the Ureter (Feiner)

1. Fistula (causative injury not stated):	
a. Ureterovaginal	91
b. Uretero-abdominal	8
c. Combined ureterovaginal-uretero-abdominal	1
2. Severed	55
3. Resected	13
4. Partially severed	16
5. Ligated	18
6. Clamped	10
7. Interference with blood supply	6

Symptoms of Ureteral Injury. Rupture or incision of the ureter permits the urine to extravasate into the adjacent tissues, producing local and general symptoms which may vary considerably, according to the location and extent of the injury. Rupture with extravasation is always a grave accident, but particularly so in the presence of virulent organisms, as an abscess, phlegmon, or even a general septicemia may rapidly result.

Pain is usually the first local symptom of rupture of the ureter. If the injury has occurred during the injection of pyelographic solution, the pain is usually sufficient to cause the patient acute suffering when only 2 or 3 cm. of solution have been injected. It may shortly subside into a dull ache, and may pass away completely within a few days, depending partly on the location of the injury and the extent to which it has permitted urine to escape into the surrounding tissues. Tenderness and rigidity over the affected side are usually marked and continuous, and large doses of sedatives or narcotics are sometimes required to relieve the painful spasms. Diminished urinary output may be noted, but this sign varies greatly in accordance with the extent to which excretion from the corresponding kidney is inhibited. Hematuria may occur, but is inconstant and therefore unreliable as a diagnostic indication of ruptured ureter. Abdominal distention is an early and constant symptom of ureteral rupture, and is probably due to retroperitoneal irritation caused by extravasated urine. Tumefaction is usually a late manifestation, and the establishment of its existence is often difficult because of muscular rigidity and spasm.

General symptoms of rupture or penetration of the ureter include

intermittent chills and fever, which may not occur until the condition has persisted for some time, when infection or toxic absorption from the extravasated urine will be in evidence. Nausea and vomiting are common at first but may cease after the lapse of 24 to 36 hours. The patient will usually lie in bed with the leg of the affected side drawn toward the abdomen, to relieve the contraction of the ilio-psoas muscle due to irritation. Any or all of these symptoms may be absent, their manifestation being inconstant and depending upon the location and extent of the injury.

Accidental ligation or severance of the ureter during surgical operation is frequently recognized at the time it occurs, and immediate repair undertaken. This, of course, is the ideal procedure. Often, however, the injury remains unobserved, the wound is closed, and the partial or complete anuria which soon follows is attributed to postoperative shock or to some other plausible cause. If but one ureter has been occluded, and the kidney and ureter of the opposite side are healthy, the condition may go undiagnosed until a fistula brings about incontinence or there is other untoward manifestation. Remotely, there may be lumbar pain and *intermittent* hydronephrosis, with other evidences commonly attributed to infection of the urinary tract, but unless pyelography is done the actual reason for the infection will not be brought out. In other cases, urinary extravasation early suggests injury to the ureter.

Anuria observed in conjunction with inability to pass a catheter should always suggest occlusion or severance of the ureter. If the anuria is complete, the injury may be bilateral; or there may be unilateral injury with a seriously impaired or functionless kidney on the opposite side.

Diagnosis. The means of diagnosing a rupture or penetration of the ureter are the same, whether the injury be due to external trauma or to injury from within. Often the diagnosis is suggested by the history and readily confirmed by excretory urography.

If the rupture has occurred during the making of a ureteropyelogram, the extravasation will be immediately apparent.

If ureteral injury can be diagnosed by other means, ureteral catheterization should be studiously avoided, because an injured ureter is much more liable to infection than an intact one. The most important diagnostic evidence obtainable is from excretion urography. Not only does this clinch the diagnosis of ruptured ureter, but it also provides indications for treatment. Should the opaque medium appear to have extravasated outside the ureter, it is a foregone conclusion that urine is likewise passing

out by the same route, and the necessity for surgical drainage of the affected area is apparent. Pain and local tenderness over the ureter, if continuing for more than 24 hours after a stricture has been dilated or some other intraureteral instrumentation has been carried out, should at once suggest the possibility of a rupture or puncture of the ureteral wall, and call for immediate investigation.

If there is reason to fear that the ureter has been injured during a surgical intervention, it will usually be a comparatively simple matter to dissect it out so as to expose the portion which may possibly have been traumatized. The possibility of severance or ligation of one or both ureters should always be borne in mind when dealing with a postoperative anuria. Inability to catheterize the ureter is, of course, suggestive. Intravenous urography is particularly useful in making the diagnosis.

If the injury has gone unnoticed to the fistulous stage, the diagnosis may be more difficult. If the fistula opens through the operative wound, there may be a urinous odor to the dressings, or the urine may emerge from the wound in spurts timed to ureteral peristalsis. In other cases, the presence of urine in the wound exudate may be detectable only after the oral administration of methylene blue. If the fistula be uretero-vaginal, there will be more or less urinary incontinence. Sometimes the orifice can be seen with the speculum. If very minute, its discovery will be facilitated by administering methylene blue and watching for the appearance of the colored urine through the speculum. The condition must, however, be differentiated from vesicovaginal fistula. Cystoscopic inspection after intravenous injection of indigo-carmin will facilitate the location of the fistula and its differentiation from other types of urinary fistula. The wisdom of passing a catheter into a ureter suspected of being injured is questionable. Some advise very cautious introduction of a soft-rubber instrument, without making the least effort to advance it once it has met with an obstruction; an opaque medium can then be injected through it and roentgenograms made. Sometimes the catheter will pass all the way to the renal pelvis despite the existence of the fistulous opening, indicating an absence of inflammatory reaction and a minimum formation of scar-tissue. Unfortunately, however, the tip of the catheter is much more likely to pass through the fistulous opening and possibly curl up in the pathological cavity which has opened out behind the injured area.

In cases where the ureteral injury has not led to fistula-formation, there is often a considerable interval between the operation and the

appearance of symptoms produced by the trauma to the ureter. The patients usually seek relief from intermittent or continuous lumbar pain of varying degrees of severity. Examination discloses a renal condition which is likely to be diagnosed as hydronephrosis without a careful consideration of the operative history. Cystoscopy with attempted ureteral catheterization will perhaps show obstruction or stricture of the ureter close to its insertion in the vesical wall. If a ureteropyelogram is made at this time, it will probably show a stricture at the level of the superior strait, the most likely place for the ureter to have been included in a ligature during removal of the uterus and ovaries. The ureter will usually be dislocated considerably from its normal position.

Prognosis. The prognosis of a traumatic injury to the ureter depends largely upon the circumstances of its occurrence. When the ureteral injury is only one of a number sustained in an automobile or other accident, it may be impossible to save the patient's life because his condition precludes proper operation for ureteral repair. A previously healthy ureter, which can be repaired or reunited over an indwelling catheter, can usually be made to heal, but there is generally some impairment of peristalsis and a strong chance of permanent dilatation.

Bilateral severance or ligation during surgical intervention throws the patient into a state of uremia, and unless quickly relieved, results fatally. Although a few cases have been reported in which the ureter appeared to have recovered perfectly, both anatomically and functionally, from an operative injury, it is doubtful if a severely traumatized duct, or one in which repair has been delayed, ever fully regains its former state. If the injury goes undiscovered, the kidney on the affected side eventually is destroyed.

Treatment. Very small nicks or cuts in the ureteral wall may heal spontaneously without treatment, or merely by introducing a ureteral catheter. Even fairly large slits and punctures will heal without suturing if given the support of an indwelling ureteral catheter, which acts as a splint to hold the ureter in proper position while it promotes healing by protecting the edges from contact with irritating urinary products.

Fortunately, as Henline has pointed out, the most common injury following ureteral instrumentation is a crack or split of a pathological ureter, requiring merely palliative treatment: rest, hot baths, forced fluids, local heat to the painful region, alkalis, and sedatives. The customary duration of symptoms is less than a week, and during this time the treatment should be conservative and expectant, with constant watching of the pulse, temperature, pain, and abdominal rigidity.

If pain and tenderness persist for more than 24 hours, an intravenous urogram will prove the best method of determining the extent of the urinary extravasation, and if this is shown to be progressing, surgical drainage should immediately be instituted. A serious clinical problem may be set up even when the urinary leakage is in itself small, for in the presence of virulent organisms, an abscess, phlegmon, or even a general septicemia may rapidly result.

The immediate and remote operative treatment of ureteral injuries is discussed under Operative Treatment of Ureteral Injuries (p. 1315).

B. DISEASES OF THE URETER

Non-Specific Ureteritis

Infection within the ureter is so closely allied with stricture and other obstructions that it is difficult to consider one apart from the other.

Primary infection of the ureter appears to be uncommon. We have seen one interesting case, in which the pelvis and parenchyma of the kidney were normal, but the attached ureter was completely filled with granulations which suggested tuberculosis. This infection was ruled out, however, and the conclusion was inevitable that the infection originated in the ureter itself.

It is highly probable that infections not infrequently arise in the ureter, run their course, and subside—all without recognition. Inflammation, in the lower section of the ureter especially, is probably responsible for a great deal of pelvic pain which is regularly attributed to other causes. The infection may be either a lymphatic invasion or secondary to a distant focus.

Non-specific ureteritis secondary to non-specific pyelitis or pyelonephritis is relatively common.

Focal infection, emphatically urged by Hunner many years ago as a cause of ureteritis, is now generally accepted as being responsible for many cases of simple chronic ureteritis, as well as of ureteral stricture. The infective focus may be in the throat or mouth, sinuses, alimentary tract, or, possibly, the prostate or seminal vesicles. It is possible that the original infection may first be arrested by the lymph nodes in the region of the ureter, the infecting organisms then being taken up by the ureteral walls, with resulting inflammation and infiltration. The infection may descend, to involve the trigone, producing distressing vesical symptoms, which usually disappear promptly upon suitable treatment of the ureteritis.

If the inflammation involves chiefly the median portion of the ureter,

the pain will be referred along the course of the duct and there will be tenderness to palpation in this region. Occasionally, the inflammation involves the entire length of the ureter. When such a condition has existed for a considerable period, the ureteral wall becomes thin and the duct dilated and elongated, resembling a worn-out rubber tube which has lost its elasticity.

The colon bacillus is the organism most commonly isolated in non-specific ureteritis. Other bacteria—staphylococci, streptococci, enterococci, proteus bacillus, typhoid bacillus—may excite ureteritis and cystitis, but in the great majority of cases it is the *B. coli* communis or communior which is found. The clinical picture of a colon bacillus infection varies considerably. In the more severe cases, microscopic examination of the urine is usually sufficient to establish the diagnosis, since pus cells and bacteria will be abundant. The preponderance of colon bacilli over all other types of organisms found in the ureter is attributed by Vermooten to the fact that other common etiological agents, such as the streptococcus and staphylococcus, are soon lost when the secondary invader makes its appearance. Only by examining and culturing a specimen of urine within a few hours of the onset of the disease, therefore, can the true causative agent be discovered.

Treatment. The treatment consists in (1) the removal or alleviation of the primary focus of infection in the kidney, bladder, respiratory tract, intestine, etc., and (2) measures directed to the relief of the local inflammation, such as rest, the application of heat to the region of the ureter, alkalis, moderate forcing of fluids, bladder irrigations, the removal from the diet of irritating foods, and chemotherapy—usually with one of the sulfonamide drugs. If the inflammation is due to an impacted stone or stricture, treatment must, of course, be directed to these causative factors.

Ureteritis Cystica

Ureteritis cystica is a definite pathological condition characterized by the formation of multiple small cysts of the ureteral mucosa or submucosa. The disease may also involve the bladder (cystitis cystica) and the renal pelves (pyelitis cystica); indeed, the lesions often appear to originate in the bladder and involve the ureters secondarily. The first mention of such a condition was made by Morgagni in 1761. Morse (1928) found that not more than 60 cases of pyelitis cystica, ureteritis cystica, and cystitis cystica, had been reported in the literature. Numerous cases have been reported since, and it is our impression that the condition is more common than the paucity of reports would indicate.

Etiology. The formation of these cysts has been attributed by various investigators to (1) central degeneration of the epithelial cell nests of von Brunn; (2) secretory activity of the epithelial cell nests; (3) inflammatory closure of crypts in the mucosa; (4) inflammatory occlusion of anomalous glands in the upper urinary tract; (5) parasitic invasion (bilharziasis).

Most investigators believe that the cysts originate from the epithelial cell nests of von Brunn, the theory advanced by von Limbeck in 1887 and von Brunn in 1893. There are two conflicting theories, however, as to the formation of these cell nests, namely: (1) they are inflammatory in nature, and are formed by downward proliferation of the epithelium, or proliferation of the connective tissue upward between the epithelial cell nests to cut off islands of epithelial cells; (2) they are sometimes found in the normal urinary tract, and may occur as congenital rests. Morse, in 125 autopsies, found cell nests of von Brunn in 108, and in 63 there was evidence of inflammation, shown by lymphatic infiltration or increase in fibrous tissue. He believed the cell nests and buds to be inflammatory in nature and not normal to the urinary tract, and concluded that these urinary-tract cysts were formed from the epithelial cell nests by a process of central degeneration rather than secretory activity. The epithelial structure of the cysts appeared incontestable to Chevassu (1936), who concluded that these ureteral formations are only "exaggerations of the epithelial cell masses sometimes seen under the mucosa of the renal pelvis and of the ureter—masses which have been called 'ureteral glands' by some authors and, more correctly, 'epithelial rests' by von Brunn."

The prevailing opinion is that the alterations in the epithelium are inflammatory in nature, and may develop in the course of any long-standing chronic irritation.

Patch (1938) inclines strongly to the view that a metaplastic process is responsible for the production of pyelitis, ureteritis, and cystitis cystica, and that in its further development it may end in cystitis glandularis and even in malignancy.

Pathology. The condition is characterized by the formation of numerous small cysts in the mucosa or submucosa. These project into the lumen of the ureter and may cause a constriction of the duct. The cysts may appear singly or grouped, are round to ovoid, and vary in size from that of a millet seed to that of a cherry stone. They are lined by a single or double layer of epithelium. In their early stages they are usually translucent, and contain a clear serous fluid. Later they become hard and grayish-yellow in color, and are filled with a yellowish-white colloid-

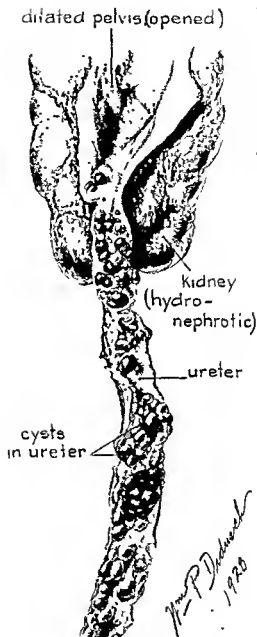


FIG. 278. Ureteritis cystica. (Christeller.)

like material. The masses are entirely intraureteral, and except for a slight dilatation at the points where the cysts are located, produce very little change in the external appearance of the ureter.

The condition has a definite tendency to bilaterality, and occasional cases have been reported in which the bladder, both ureters, and both renal pelves were involved. Stow (1907) reported a case of bilateral double ureters, in which each of the four ureters, from its origin to within 4 cm. of its entrance into the bladder, was thickly studded with cysts of varying sizes

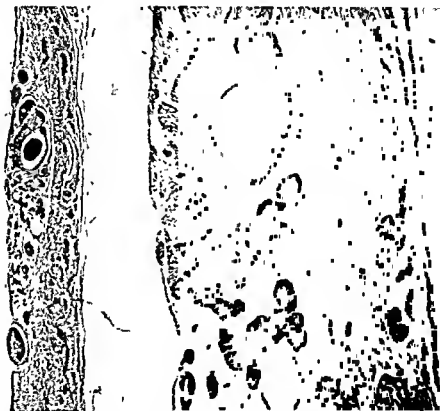


FIG. 279. Case of ureteritis and pyelitis cystica. (1) Low-power photomicrograph. (2) High-power photomicrograph. Note the numerous small cysts distributed over the mucosal lining of the ureter

Symptoms and Diagnosis. *The symptoms are not pathognomonic, being those of the underlying cause of the cystic changes—usually calculus or chronic infection. Larger cysts may occlude the ureteral lumen sufficiently to cause serious obstruction. Copious hematuria is occasionally reported. The bacterial flora is quite varied in these cases, but without any special significance*

Prior to 1929, when Jacoby and Joelson each diagnosed a case by

pyelography, cases of ureteritis and pyelitis cystica were discovered only at autopsy or at operation for other causes. Patch (1938) was able to collect from the literature only 8 cases in which the diagnosis of pyelo-ureteritis cystica had been made *clinically*, to which he added 2 personal cases.

The diagnosis is quite easily made by retrograde or excretory urography, which will show a characteristic bubbly or frothy appearance of the ureter through more or less of its extent, due to displacement of the opaque medium by the cysts. Dilatation, tortuosity, or constriction of the ureter is common.

Ureteritis and pyelitis cystica are frequently associated with cystitis cystica; therefore, when cystitis cystica is noted on cystoscopic examination, the upper urinary tract should receive careful investigation.

Treatment. Treatment should be directed to the removal of the underlying irritative factor.

Symptoms of obstruction, due to constriction of the ureter or blockage of its lumen by the hulging cysts, have been relieved in some cases by repeated ureteral dilatations, followed by the injection of silver nitrate, in a 1 or 2 per cent solution. Kindall suggests passing a large ureteral catheter to the renal pelvis and permitting it to remain for 3 days. This results in mechanical rupture of the cysts, the walls of which are highly friable.

If conservative measures fail, and there is serious impairment of the kidney function, nephro-ureterectomy may be required. In such cases, very careful investigation of the contralateral kidney and ureter is necessary, because of the tendency of the cysts to be bilateral.

Ureteritis Granulosa

Ureteritis granulosa is an uncommon condition characterized by the formation of localized areas of granulation tissue in the ureteral mucosa and submucosa similar to those not infrequently seen in the bladder, urethra, and renal pelvis. The granulomatous areas may be merely slightly elevated patches upon the mucosa, but more often appear as polypoid growths which bleed profusely and are likely to be confused with malignant neoplasms.

Etiology. The etiology has been variously ascribed to (1) the occurrence of lymph tissue in the mucosa of the urinary tract (Chiari); (2) an accumulation of round cells (Stoerk); (3) round cells of inflammatory origin in conjunction with true lymph follicles (Paschkis).

Pathology. Granuloma of the ureter is seldom found except at operation or autopsy. When the ureter is opened, localized areas in both the mucous membrane and the submucosa will be observed. Sectioning and examination of these will show granulation tissue, with infiltration of large and small mononuclear cells, intermixed with occasional polymorphonuclear leukocytes. The microscopic picture is that of a definitely benign process, and readily differentiates the lesion from the malignant neoplasm that it is invariably suspected of being.

Symptoms and Diagnosis. There are no characteristic symptoms. Hematuria regularly occurs, and may be profuse. The passage of clots may induce pain simulating renal colic. If secondary infection is present, the characteristic manifestations—frequency, dysuria, rise of temperature, and chills—will be in evidence. Urinalysis is likely to show pus and blood, as well as organisms such as the colon bacillus and *Staphylococcus aureus*. These manifestations, however, are all common to many other pathological conditions of the urinary tract.

Ureteropyelography can only show the presence of a pathological lesion in the ureter, but cannot differentiate it from the malignant one which is usually suspected. Malignancy must therefore be assumed until it is possible, usually by operation, to prove the benign nature of the growth. Single or multiple circumscribed filling defects, together with a possible ragged appearance of the ureteral edges, may suggest tuberculosis, but this can be ruled out by repeated urinalysis. Braasch was able to make a diagnosis because the affected tissue was situated low down in the vesical end of the ureter, where it could be detected cystoscopically and a piece of tissue secured with a cystoscopic rongeur.

Granuloma of the ureter is apparently extremely rare, and its chief clinical importance lies in the establishing of its benign nature when malignancy of the ureter is in question. The diagnosis must therefore rest solely upon the pathologist's findings.

Prognosis. The prognosis is, in general, that of other benign growths in this location. Any obstruction to renal drainage menaces the integrity of the kidney, and is, therefore, a threat to health and to life.

Treatment. As no means of establishing a preoperative diagnosis are available, treatment must be symptomatic until the ureter has been surgically approached. Sometimes hemorrhage may be so severe as to exsanguinate the patient and make immediate operation imperative. Most of the recorded cases were treated either by excision of the affected part of the ureteral wall and anastomosis, or by nephrectomy. Where

biopsy can first be done, a good kidney may be saved, and, needless to say, every effort toward this end should be made.

Leukoplakia of the Ureter

Leukoplakia of the ureter is practically never seen except at autopsy or at operation for some related condition. Only a few cases primary to the ureter are on record. Of 152 cases of leukoplakia of the urinary tract reviewed by Patch (1929) 36 involved the renal pelvis, 6 the ureters, and 110 the bladder. Extension of vesical leukoplakia into the ureters appears to be exceedingly rare; but ureteral findings in cases involving the renal pelvis are relatively frequent. It seems probable that leukoplakia affects the ureter, primarily or secondarily, more often than the meager data offered by the literature would suggest.

Etiology. The etiology of leukoplakia of the urinary tract is discussed under Leukoplakia of the Bladder (p. 1019).

Pathology. The lesion in the ureter consists of deposits of cornified squamous epithelium upon the ureteral mucosa. The epithelium undergoes keratinization, giving it a definitely epidermoid character. In the ureter and renal pelvis these cornified patches appear as elevated, dull, grayish-white membrane, their surfaces lying in well-defined rugae. The patches may become confluent, so that the duct appears to be lined in more or less of its extent with a whitish membrane, which is dissected free with difficulty. In one of the recorded cases autopsy showed that in some spots in the ureter the cornification almost completely blocked the lumen.

Microscopically, these cornified plaques resemble normal skin, presenting the typical strata observable in a section of epidermis. The connective tissue underlying these strata shows lymphocytic infiltration, doubtless produced by the inflammation upon which the lesion depends.

From the few recorded cases it would appear that there is a definite tendency for the ureteral condition to be bilateral.

Diagnosis: Prognosis: Treatment. For the diagnosis, prognosis, and treatment of leukoplakia the reader is referred to Leukoplakia of the Bladder (p. 1019) and Renal Leukoplakia (p. 1529).

Specific Infections of the Ureter

GONORRHEA

Incidence. Although involvement of the bladder neck and trigone is a common complication of gonococcal posterior urethritis, a general-

ized gonococcal cystitis is unusual and infection of the upper urinary tract distinctly rare. Some idea of its infrequency is gained from the fact that Sisk and Wear (1930) were able to collect from the literature only 30 authenticated cases—including kidneys, ureters, and bladder.

Etiology. Apparently, gonorrhea infects the ureter only secondarily, and in most instances is an extension from a gonococcal cystitis. We have never seen a case where gonococcal infection could be demonstrated in the ureter independent of an immediately adjacent focus in the bladder. It is reasonable to assume that in the presence of a gonococcal cystitis or trigonitis infection may extend to the ureters, renal pelves, and even to the kidneys themselves. In cases with involvement of the upper tract, secondary pyogenic organisms, such as *Bacillus coli* and staphylococci, are often found.

Symptoms and Diagnosis. Such an infection is likely to be chronic or subacute rather than acute. Only when there is associated inflammation and obstruction to the outflow of urine in the lower part of the urinary tract is there likelihood of the ureter being included in the gonococcal infection, and under such circumstances the inflammation is apt to be bilateral.

The symptoms of ureteral gonorrhea are not characteristic. There may be slight rise of temperature, and pressure on the angle formed by the lowest rib and the erector spinae muscle may elicit slight tenderness. Intermittent or constant pyuria may be present. Cystoscopic inspection will show the ureteral orifices to be inflamed and patulous, with a little pus oozing from them in most cases.

The demonstration of the gonococcus in the ureteral discharge or urine sediment is sufficient to establish a positive diagnosis. This is usually easy in acute cases, in which large numbers are present; but in chronic cases, and particularly in mixed infections, identification of the gonococcus may be difficult. In such cases cultures are of great value.

Treatment. Since gonococcal ureteritis is secondary to gonococcal urethritis and cystitis, its eradication depends upon cure of the infection in the lower urinary tract (see Gonorrhea: Treatment, p. 717).

SYPHILIS

Syphilis of the ureter, like gonorrhea, is apparently excessively rare and usually a secondary invasion. Valverde (1923), however, reported a case of gumma in an hereditary syphilitic which he regarded as primary to the ureter, there being no apparent involvement of either the bladder

or the kidney. No case of ureteral syphilis, either primary or secondary, has been observed by us; and despite the advances in knowledge of all phases of syphilis, and the improvements in laboratory technic, modern urological literature makes no mention of its occurrence.

BILHARZIASIS

Bilharziasis of the urinary tract is due to invasion by the parasite *Schistosoma haematobium*. The etiology, pathogenesis, pathology, diagnosis, and treatment of this infestation are considered at length under Diseases of the Bladder (Bilharziasis, p. 1030).

Under etiology, it is noted that the parasites mature in the portal vein and the symbiotic pairs migrate to the pubic and vesical plexuses. Here the females lay large numbers of eggs, which are deposited, for the most part, in the base of the bladder and the terminal portion of the ureter. Although any part of the urinary tract may be affected, lesions of the urethra and renal pelvis are uncommon. Lesions confined to the ureter alone are also rare. However, in the so-called bilharzial countries, vesical bilharziasis is very common, and in a high percentage of these cases there is involvement of the lower ureter. Serious complications frequently follow: stricture of the ureter, fistula, tortuosity, hydronephrosis, pyonephrosis, lithiasis, malignant neoplasms.

Diagnosis of Ureteral Bilharziasis. Bilharziasis of the urinary tract is diagnosed mainly by (1) examination of the urine, particularly for ova; (2) cystoscopy; and (3) roentgenography.

In most cases of urinary bilharziasis the urologist is first consulted 8 to 10 years after the original infestation, at which time ova are rarely present in the urine. The cystoscopic appearances of the various manifestations of bilharziasis have been described under Vesical Bilharziasis; as a rule, these are easily recognized by those familiar with the disease.

Ureteral bilharziasis is best demonstrated by pyelography. As bilharzial complications not infrequently prevent the use of the ureteral catheter, intravenous urography is often preferred. In some cases, diagnosis can be made during life only by means of roentgenograms. These are the so-called "closed" bilharzial infections, in which the eggs are deeply deposited in the submucous and muscular layers and do not penetrate the mucosa, so that there is absence of clinical manifestations—for example, hematuria and ova in the urine—and of macroscopic changes in the mucosa.

Affi (1930; 1934) called attention to "cloud-like shadows" and "calci-

fied demarcations" of the lower ureter and bladder in cases of long-standing bilharziasis. This dense cloudy shadow is due to the "general thickening of the layers of the affected part of the urinary tract on account of the presence of calcified eggs regularly deposited but not of sufficient number or concentration to throw a denser calcareous shadow of the organ." This cloudy appearance, though highly suggestive of bilharziasis, is not absolutely diagnostic, as other conditions may give it. The calcified demarcations, however, this author considered pathognomonic. They often appear in the radiogram as shadows as dense as osseous tissue, and may outline the ureter, bladder, or urethra. They are caused by infiltration of the ureter, or other part of the tract, by calcified ova.

Vermooten (1937) pointed out another roentgenographic finding, which he regards as pathognomonic of ureteral bilharziasis in its later stages—namely, dilatation and tortuosity of the lower (pelvic) ureter associated with a normal lumbar ureter, normal pelvis, and normal calyces. The occurrence of these pathological changes he explains as follows: In ureteral bilharziasis the ova are usually found in the pelvic portion of the ureter, resulting in narrowing and obstruction of the intramural portion (which, for mechanical reasons, cannot dilate) and dilatation and tortuosity of the remainder of the infested portion (the pelvic third) while the uninfested upper portion remains normal. With increasing obstruction, the entire upper urinary tract will eventually also become dilated. These pathological changes in the lower ureter, associated with a normal, or slightly dilated, upper tract, Vermooten found to be quite common, and, as bilharziasis is the only disease that infests primarily the pelvic ureter without affecting the upper portion, except in rare instances, may be considered as pathognomonic.

Treatment. Treatment of bilharziasis consists of the intravenous injection of tartar emetic or the subcutaneous administration of antimony tartrate (Bilharziasis, p. 1034). Late sequelae, in the ureter or bladder, require appropriate treatment. Nephro-ureterectomy is not infrequently necessary when there is extensive cicatrization and narrowing of the ureter with resulting hydronephrosis or pyonephrosis.

ACTINOMYCOSIS

Actinomyces rarely affects any portion of the urinary tract. Occasional cases of bladder, kidney, or bladder and kidney infestation have been recorded, but we have been unable to discover any instance of its primary occurrence in the ureter. When the spores are disseminated

by the blood stream, secondary infection can take place, and occasionally, in cases of vesical and renal involvement, the communicating ureter shares in the pathological process. However, it is notable that in several detailed autopsy reports it is distinctly stated that the ureter was entirely normal. In Stanton's case, where both kidneys and the bladder were extensively infected, the left ureter was found to be normal and the right contained "a thin, cloudy fluid."

For the diagnosis and treatment of actinomycosis, see Actinomycosis of the Bladder (p. 1035); of the Kidney (p. 1525).

ECHINOCOCCUS DISEASE

Echinococcus disease (hydatid disease) of the urinary tract is rare, and is confined chiefly to the kidney (Echinococcus Disease of the Kidney, p. 1520). A few cases of hydatid cyst originating in the renal pelvis and extending into and obstructing the ureter have been reported.

In Escat's case the cyst undoubtedly originated in the renal pelvis and extended into the ureter. The patient was pregnant when it was first discovered, but with great care she was carried to full term. Later, the kidney was taken out, but microscopic examination indicated that the infestation had always been confined to the pelvis, whence the cyst had ruptured and poured its contents into the ureter. In the case of Delanglade (cited by Escat) there was a hydatid cyst "about as big as an egg" obstructing the left ureter and the passage of numerous daughter cysts from the other ureter. It was apparently assumed that all the cysts originated in the renal pelvises.

TUBERCULOSIS OF THE URETER

Etiology. It is commonly accepted that only secondarily is the ureter infected by tuberculosis. Recently, however, Ljunggren and Wahlgren reported the case of a 17-year-old girl in whom no focus elsewhere in the urogenital tract could be found. *The patient had a bilateral pulmonary infection, and the authors believe the ureteral infection to have been an instance of direct hematogenic origin, though they admit that the case also offers support to the theory of "tubercle bacilluria"—that is, the excretion of the infecting organisms through an anatomically intact kidney.* A few other cases of supposedly primary ureteral tuberculosis have been reported, but the lesion is very rare and of slight clinical importance in comparison with tuberculous ureteritis that is secondary to a focus in the kidney or part of a generalized urogenital tuberculosis.

It is, of course, probable that, granting that tuberculosis of the kidney arises from hematogenous infection, a primary focus can be implanted in the ureter in the same way. Against this theory of blood-borne infection, however, is the great preponderance of unilateral cases of renal and ureteral tuberculosis, lending weight to the belief that tuberculosis of the ureter most commonly is a descending infection from a focus in the kidney which it drains. Tubercle bacilli are carried down from the kidney and implant themselves upon the ureteral mucosa, producing the characteristic tuberculous lesions. Where the kidney has been diseased for a considerable period of time, the ureter is likely to participate in the tuberculous infection. Sometimes, however, one sees patients with extensive lesions in both the kidney and bladder in whom the ureter is free of disease.

While descending infection from the kidney is probably the etiological factor in most cases, the ureter may also become involved by extension through the lymphatics or by continuity from the bladder below. Tuberculous cystitis may impair the integrity of the ureterovesical "valve" permitting urinary reflux and the implantation of tubercle bacilli in the ureteral wall.

Pathology. With invasion of the ureteral mucosa by tubercle bacilli, tubercle-formation takes place, the process later extending to the muscularis and periureteral tissues, resulting in narrowings and even strictures. Later, caseation takes place, with occlusion of the lumen by caseated material; and still later the entire ureter may be transformed into a solid fibrous cord with a non-functioning kidney above.

In later stages of the tuberculous process the ureteral changes may be diffuse and involve the entire duct; but the initial involvement is usually at either the vesical or the pelvic end, nearest the source of infection.

Symptoms: Diagnosis: Treatment. For the symptoms, diagnosis, and treatment of ureteral tuberculosis the reader is referred to *Tuberculosis of the Kidney* (p. 1487). ●

Urography is frequently of great assistance in making a diagnosis. Calcium deposits occur less frequently in the ureter than in the kidney, but when present, may involve a considerable portion of the duct—often the lower portion. The shadow may be several centimeters in length and outline the dilated ureter to a greater or less extent. The shadow is caused either by calcareous deposits in the thickened wall of the ureter or by deposits in the ureteral lumen. There is often a peri-

ureteral infiltration which, together with the thickened ureter, will cause a tumor mass that frequently can be palpated on rectal or vaginal examination.

Tumors of the Ureter

Tumors—benign or malignant—arising *primarily* from the mucous membrane of the ureter are uncommon.

Secondary tumors of the ureter are much more common. The most frequent are implantations from an original papillary carcinoma of the renal pelvis, but the ureter may also be involved by dissemination of tumor from the bladder, or by direct extension of cancer from a neighboring organ—most commonly the cervix, bladder, or sigmoid colon. Secondary involvement from blood stream or lymphatic metastases also occurs.

PRIMARY TUMORS OF THE URETER

Etiology. The etiology of primary tumors of the ureter is obscure, but it is probably closely related to that of vesical tumors. Etiological factors that have been suggested are: (1) leukoplakia with malignant metamorphosis; (2) cell inclusions occurring during embryonal development and adult life; (3) chronic inflammatory irritations; (4) benign hyperplasia of the mucous membrane; (5) mechanical irritation, particularly that due to calculus. In a considerable number of the recorded cases of malignant tumor, and in several cases of benign tumor, there was coexisting calculus, and stone is regarded as an important etiological factor in tumor development.

Pathology and Incidence. Histologically, primary tumors of the ureter correspond exactly to those of the bladder and renal pelvis. The most common types are papillomas—benign and malignant. Squamous-cell carcinomas are rare, highly malignant, and more apt to be associated with stone. A few sarcomas have been reported.

Primary benign tumors are even rarer than malignant neoplasms. In a comprehensive review of the literature in 1932, Melicow and Findlay were able to collect only 28 acceptable cases, to which they added one of their own. Four of these were fibromas; the remainder papillomas.

Although the marked progress in the technic of urological diagnosis and the tendency toward more frequent and careful autopsies have resulted in the finding of primary carcinoma of the ureter with ever-increasing frequency during recent years, this form of neoplastic disease must still be ranked as relatively rare. Only 1 case of proved primary



FIG. 280. Polyps of the ureter, with slight hydronephrosis. (Courtesy of Dr. Marion, Service Civile, Hôpital Lariboisière, Paris.)

ureteral cancer was found in 22,810 autopsies performed at Bellevue Hospital (New York) from 1904 to 1935, and up to 1930 no case had

been observed at the Memorial Hospital (New York) in a study of 16,565 malignant tumors. The case reported by Snyder and Wood in 1933 was the first ever seen at the Massachusetts General Hospital, one of the oldest institutions in the country. Foord and Ferrier (1939) estimate that about 1 per cent of carcinomas of the upper urinary tract originate in the ureter. The majority of these are papillary carcinomas.

The first reported case of primary carcinoma of the ureter, with microscopic diagnosis, was that of Wiesing and Blix, recorded in 1878. Albert M. Crance, reporting an interesting case of primary carcinoma (epithelioma) in 1924, was able to find only 27 previously recorded cases. The literature has been thoroughly gone over a number of times in recent years. Excellent reviews were made by Kretschmer (1924), who reported 36 cases; Player (1928); Rousselot and Lamon (1930), who found 50 cases; and W. W. Scott (1934), who found 59 cases and added 2 more. Scott's report is particularly valuable for its study of the remote results. The 61 cases reviewed by him were classified, histologically, as follows:

Type of Growth (Original Diagnosis):

	<i>Number</i>
Papillary carcinoma	36
Squamous-cell carcinoma	9
Medullary carcinoma	7
Solid carcinoma	3
Carcinoma simplex	3
Adenocarcinoma	1
Cylindrical cell carcinoma	1
Transitional-cell carcinoma	1

Schillings and Sondervorst (1936) tabulated 113 cases of primary malignant tumors and added 2 of their own. Foord and Ferrier (1939) added 10 cases from literature which had never been included in previous compilations and 6 of their own. During the past 5 years the reported cases have been fairly numerous, and the volume of literature is at present quite formidable. Approximately 160 cases of primary malignant tumors of the ureter have been reported to date.

In view of the structure and function of the ureter, it is inevitable that any type of ureteral neoplasm should rapidly cause urinary obstruction, with the regular accompaniment of dilatation, hydronephrosis and infection, and eventual destruction of the involved kidney, and such is the case with the majority of ureteral tumors.

Generalized metastases by way of the blood stream occur fairly early. The liver, lungs, and bones are the structures usually involved. The tumor may involve the retroperitoneal vessels, seminal vesicle, bladder,

and other nearby structures by extension. Implantation may occur into the remaining portion of the ureter or the bladder.

Both benign and malignant tumors occur with about equal frequency in the fifth, sixth, and seventh decades of life, and are seen more frequently in men than in women. The right ureter is involved slightly oftener than the left. In almost three-fourths of the recorded cases of primary tumor the growth involved the lower ureter. Occasional cases have been seen where both the upper and lower ureter contained papillomatous growths, with no apparent involvement of the intervening portion.

Symptoms. The chief symptoms of ureteral tumors—hematuria, pain, and a palpable tumor mass—are not in the least pathognomonic.

Hematuria is the earliest and most striking symptom, occurring in three-fourths of all cases of both benign and malignant tumors. The bleeding is at first intermittent and slight in amount, but as the growth develops the hematuria occurs more frequently and increases in amount. Worm-like clots may be passed, and profuse hemorrhage is not uncommon—particularly upon the passage of a ureteral catheter.

Pain is the next most prominent symptom, occurring in over 65 per cent of cases. Due to early occlusion of the ureteral lumen by the growth, hydronephrosis is an early complication. In many cases pain is due to the presence of a hydronephrotic kidney, and consequently takes the form of a dull constant ache in the kidney region. In an advanced stage of the disease, when there may be invasion of the pelvic nerves, the pain may be referred to the sacral and lumbar regions, thigh, or hip. The passage of clots may produce an acute colic. Benign tumors are in themselves painless, and pain, when present, is almost always due to a progressive hydronephrosis.

The tumor itself is generally not palpable, although there have been cases in which the growth could be palpated on either abdominal, rectal, or vaginal examination. In almost one-half of the recorded cases, however, there was a palpable mass due to a hydronephrotic kidney.

Urinalysis usually shows pus and red blood cells, and examination of the centrifuged sediment may disclose atypical cells or detached papillomatous villi.

Diagnosis. The positive diagnosis of ureteral tumors may be very difficult, and when made, usually depends on the history and physical examination, cystoscopy, ureteral catheterization, and pyelo-ureterography. Even with these diagnostic aids, a ureteral tumor is easily over-

looked since calculus, stricture, hydronephrosis, or pyonephrosis frequently is associated.

Cystoscopic inspection may give valuable information (1) by demonstrating the side from which the bleeding occurs, or (2) by showing the tumor protruding through the ureteral orifice, or secondary implants close to the ureteral orifice, suggesting the presence of a primary tumor higher up.

Ureteral catheterization nearly always suggests the diagnosis, as in a majority of cases the catheter's tip is stopped or obstructed when it reaches the tumor. Persistent, profuse bleeding after a catheter has met an obstruction in the ureter should lead one to suspect a ureteral neoplasm. However, calculus, trauma, and infection must be ruled out.

While ureterograms are not sufficiently characteristic to enable one to make a diagnosis of ureteral neoplasm by this means alone, the information they yield is frequently very valuable when added to the evidence in favor of such a diagnosis obtained from the history, physical examination, and cystoscopy. In cases in which calculus and traumatic or tuberculous stricture have been ruled out, a ureterogram showing an obstructed ureter, with dilatation above the point of obstruction and an enlarged kidney pelvis with no filling defects such as those seen in primary carcinoma of the renal pelvis or parenchyma, suggests the possibility of primary tumor of the ureter. This is especially true if there has been a history of hematuria and if, on cystoscopic inspection, there is profuse bleeding from the involved side following ureteral manipulation.

Because of the very high mortality of ureteral tumors in the later stages, and the relatively early occurrence of metastases, exploratory operation would seem to be justified in cases in which the diagnosis is strongly suspected but cannot be proved.

Prognosis. Radical operation has proved the only effective treatment; but the prognosis is poor, even in the relatively favorable cases. In the series of cases reported by Scott, the primary mortality was 27 per cent, and of the cases followed over a long period only 2 patients were well 5 years after operation. A. W. Hunter has subsequently reported another case in which the patient survived operation for papillary carcinoma for 6 years, death being due to a colloid cancer of the stomach. These are the only five-year cures that have been reported. All 3 cases were correctly diagnosed preoperatively. Nephro-ureterectomy was performed in the first, and second cases, and ureterectomy in the third.

Benign ureteral tumors, like those occurring in the bladder, offer a

definite threat to life since they carry with them a strong probability of later malignancy and metastases which are rapidly fatal. Even if, histologically, they retain their benignant characteristics, their presence in the ureter will, in most cases, eventually cause hydronephrosis, with destruction of the kidney.

Treatment. The treatment of choice is complete surgical removal. Deep x-ray and radium therapy have been tried in a very few cases, but thus far have proved of little value.

The choice of operation depends upon the location and extent of the tumor and the condition of the patient. If the tumor is small and situated close to the bladder, and if the possibility of implants to other portions of the duct can be definitely ruled out, and the kidney is worth saving, the involved portion of the ureter may sometimes be resected and the remaining segment reimplanted in the bladder wall. In the majority of cases, however, complete nephrectomy and ureterectomy offers the only certain means of removal and should be done, provided the opposite kidney is functioning satisfactorily and the patient's condition permits. Upon the patient's general condition, as evidenced by the preoperative study, must be based the decision as to whether to perform a primary nephro-ureterectomy, or to remove either the kidney or ureter first and the remaining organ as soon as the patient's condition permits. Whether or not there is involvement of the bladder wall near the ureteral orifice, this area should be removed with the ureter, together with a margin of healthy tissue.

If the opposite kidney is not functionally capable of carrying on alone, ureterectomy with the performance of a permanent nephrostomy is probably the wisest choice.

Diverticulum of the Ureter

Diverticulum of the ureter is very rare (23 cases to 1936, Campbell), and has received scant consideration in the literature.

Etiology. Ureteral diverticula may be either *congenital* or *acquired*.

Congenital diverticulum, which may occur anywhere along the course of the ureter, is the rarest type (9 cases to 1936, Brown). A bifurcation with a blind ending may simulate it, and some of the reported cases are really cases of ureteral bifurcation. The etiological factor in the production of this type is evidently the failure of a portion of the ureteral bud to join with its metanephrogenic cap. Congenital diverticula are more likely to assume the shape of the ureter, simulating an appendix in ap-

pearance and size, whereas the acquired type is usually globular in outline.

Acquired diverticulum has been described as a "blow-out formation" consequent to blockage of the ureter distal to the diverticulum. Due to some inflammatory condition the ureteral wall is weakened, causing it

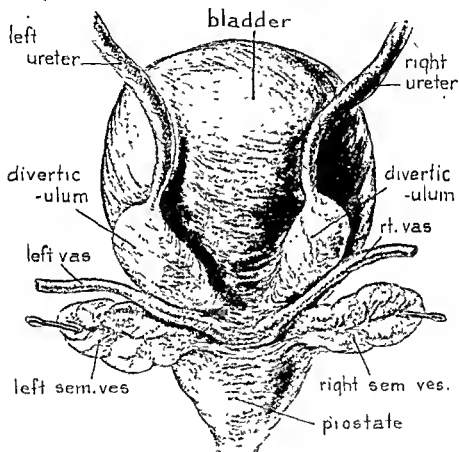


FIG. 281 Bilateral diverticula of the ureters, view of the posterior surface of the bladder. (Courtesy of Dr. Marion.)

to stretch and undergo sacculation when some unusual strain or pressure is exerted at the point of weakening. It may or may not be accompanied by the formation of stones in the ureter. The rarity of acquired diverticula may be accounted for, in part at least, by the fact that intra-ureteral pressure is normally quite low. Most of the recorded cases showed the sac in the lower third of the ureter, just proximal to the ure-

teral orifice. The condition has been frequently confused with ureterocele, but the two lesions are distinct entities and should not be classed as variations of the same pathological condition.

Symptoms and Diagnosis. The diverticulum may help to perpetuate an existing urinary infection, in which case the clinical picture will be that of a chronic pyelitis; or it may compress the ureter, resulting in dilatation of the proximal portion, when there is likely to be pain in the loin.

Advances in ureteropyelography, particularly by the retrograde method, permit the diagnosis of these pockets with greater accuracy. If the diverticulum contains calculi, they will usually be visible in the plain x-ray film. Occasionally, the passage of a ureteral catheter will demonstrate the presence of the sac, but unless the orifice is large, the tip of the instrument is likely to pass by it without opposition.

Treatment. In a few cases the mere passage of instruments for diagnostic purposes, or systematic dilatation of the diverticular orifice, has served to effect symptomatic relief.

In most instances, however, it has been necessary to resort to surgery. Excision of the sac and suturing of the defect in the wall is usually advisable. In one case, where the sac was located just behind the bladder to the left of the ureteral orifice, the sacculated ureter was exposed through a median incision over the pubis, the diverticulum excised, and the cut edges of the ureter sutured directly to the bladder mucosa. The result was excellent.

If the diverticulum is near the vesical end, the ureter may be cut off, and, after the diverticulum has been resected, the healthy ureter above reimplanted into another part of the bladder. This assumes, of course, that it is possible to do this without undue stretching of the ureter to insert it into its new opening in the vesical wall.

Ureteral Calculus

Sex and Age Incidence. In practically all large series of cases of ureteral stone that have come to our attention, as well as in our own series, the frequency of occurrence in males is considerably greater than in females, the preponderance being in a ratio variously estimated at from 2 to 1 to as much as 4 to 1. Even allowing for the fact that many cases of ureteral stone in women are treated in gynecological services, it is indubitable that men are more often sufferers from this condition than women.

As regards age, the great majority of patients are between 20 and 50 years of age. No age is wholly exempt—ureteral stones having been found in an infant of 6 months and in the very aged—but in the Western Hemisphere, at least, cases in infants and children are rarely encountered today.

Etiology. It is the generally accepted belief that most calculi found in the ureter form in the kidney and then pass down the ureter. Hunner, however, believes that calculi are formed primarily in the ureter, and contends that it is the existence of stricture which provides lodgment for the particles which form the nucleus of the stone. Others have argued that the stricture is the result—not the cause—of the stone, which originates in the kidney and migrates downward until it becomes too large to progress further. It is quite possible that both of these explanations are correct. Certainly, stricture and obstruction of the ureter would offer favorable conditions for the formation of stone directly at the site of the constriction. If the area becomes infected, there is still greater likelihood of stone-formation or rapid increase in the size of one already begun.

Many theories as to the cause of urinary calculi have been advanced, none of which is universally accepted. These have been discussed under Renal Calculus (p. 1584). The more important etiological factors are infection, stasis, a diet deficient in vitamins A and D, and faulty metabolism.

Types of Stone. Three main types of stone are found in the ureter: calcium oxalate, calcium phosphate, and uric acid stones. Most stones are of mixed composition, but usually there is a preponderance of one component. If the urine is sterile, calcium oxalate will usually predominate, but where urinary infection exists, phosphatic stones are more likely to be found. "Pure" uric acid stones are much less frequent in the upper tract than in the bladder, and the urologist is not often called upon to deal with them because, as a rule, they are small and smooth and pass without giving rise to distressing colic. The oxalates are the most opaque of the ureteral stones, but a large percentage of ureteral calculi can be demonstrated by plain x-rays.

Pathology. Stones are usually found singly in the ureter, but about 10 per cent are multiple. Bilateral stones are rarer than in the kidney.

If a stone is arrested in its progress down the ureter, it will give rise to certain special urological problems, such as diverticulum-formation at the site of impaction, or dilatation of the lumen above the stone, causing hydronephrosis or pyonephrosis; or it will induce back pressure

upon the kidney pelvis, with almost inevitable infection. The mucous membrane above the site of impaction becomes congested, and this will usually cause a hematuria, which alarms the patient and impels him to seek medical aid. Once the continuity of the epithelial lining has been broken, infection readily gains entrance.

The severity of the damage is not always proportionate to the size of the stone. A small, obstructing stone may produce greater damage than a large one which causes the ureter to dilate around it, permitting drainage of urine alongside it. Calculi have not infrequently remained in the lower third of the ureter for long periods of time without causing serious injury to the upper tract. These have had grooves in them through which the urine passed, or the urine drained around them.

Some very large ureteral stones have been reported—one (Goldman, 1932) being 18 cm. long and weighing 132 Gm.

Symptoms. The symptoms of ureteral calculus vary according to (1) the degree of obstruction, (2) the extent of infection, and (3) the condition of the kidney.

By far the most frequent symptom of ureteral calculus is pain. The pain may be due either to intrarenal tension as a result of the ureteral obstruction, or it may be evidence of an inflammatory process which follows localization of infection at the point of lodgment of the stone, or higher up in the blockaded urinary tract. Pain, located by the patient in the renal area, will therefore often be due to a stone in the ureter rather than to one in the renal pelvis.

Usually the pain is of a colicky character. The passing of a renal calculus into or through the ureter causes excruciating pain, frequently accompanied by hematuria and, in the infected cases, by the constitutional manifestations of urosepsis. The colic is due to the peristaltic contractions by which the ureter attempts to expel the foreign body. The pain originates in the renal region and radiates along the course of the duct into the groin. It is frequently agonizing, and may even cause the patient to go into shock, evidenced by sweating, pallor, fall in blood pressure, etc. When the stone is impacted high in the ureter, nausea and vomiting may be prominent features. When impacted in the middle third of the duct, the calculus may induce pain at the end of micturition—in the male often centering at the tip of the penis, in the female in the labium majorum of the affected side. If the stone is impacted low down in the ureter, the pain may be referred to the testicle, which will be found tender on palpation. Both sexes may experience pain on coitus.

Hematuria is common. It is frequently the first symptom to attract

the patient's attention, as the calculus may injure the delicate mucous membrane sufficiently to cause bleeding even before impaction takes place. Pus, albumin, and bacteria are also found in the urine. While these are not, of course, pathognomonic signs of calculus, in conjunction with the other findings they should lead to a correct diagnosis.

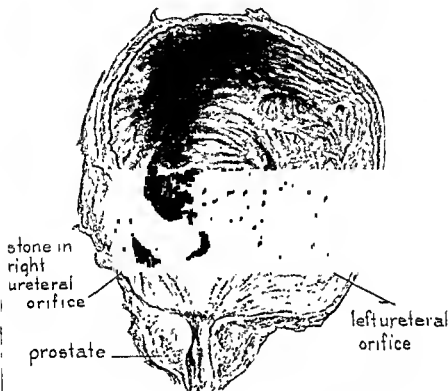


FIG. 282. Calculus at the right ureteral orifice. (Christeller.)

An impacted calculus may cause a complete obstructive anuria on the affected side, with or without reflex anuria on the other side.

Diagnosis. The diagnosis is based upon the history, physical examination, urine examination, renal function tests (to determine the extent of damage to the kidney), cystoscopy and ureteral catheterization (wax-tipped catheter), and roentgenography.

A complete history is important, since the duration of symptoms has a direct bearing, as a rule, on the treatment. A patient suffering from an initial attack of renal colic is usually treated much more conservatively

than one who gives a history of repeated attacks of acute ureteral obstruction.

Seldom are any but the largest stones detectable by palpation. A ureteral calculus can sometimes be felt through the rectum or vagina, however, and should always be sought by palpation of these passages.

Routine urinalysis will disclose the presence of blood, pus, albumin, and bacteria, if these are present.



FIG. 283. Wax-bulbed catheter showing a typical scratch from contact with a stone in the ureter. This method is of inestimable value in detecting the presence of uric acid or other non-shadow-casting calculi in either the ureter or the kidney.

Cystoscopic inspection will usually give definite evidence of the presence of a stone which is located at or near a ureteral orifice. Even when the stone is some distance up the duct, there may be a certain amount of rigidity of the orifice; or there may be pouting of the orifice, suggesting ureterocele. If the stone is in the intramural portion of the ureter, there will be swelling and edema, sometimes accompanied by hemorrhage. The amount of urine issuing from the opening may vary from none at all to a normal output. The functional ability of each side should be tested by the usual methods.

Attempts should always be made to catheterize both sides, but in the

affected ureter the tip of the instrument will usually be stopped by the stone. Sometimes, however, the catheter passes the calculus without the least sense of obstruction.

The wax-bulbed catheter is the most accurate method of diagnosis for ureteral stones which fail to show in the x-ray, but great care must be exercised to make sure the scratches on the catheter are made by the stone.

Radiography is the most valuable aid at the urologist's command for the diagnosis of ureteral stone, and the one upon which he places his main reliance. There are three types of radiographic investigations that may be carried out in suspected cases: plain roentgenography, retrograde pyelo-ureterography, and excretion urography.

Unless composed of urates or uric acid, a large percentage of ureteral calculi can be demonstrated by plain x-rays. False shadows, cast by phleboliths, bowel contents, warts on the skin, artifacts in the plates, etc., must be ruled out. In women suffering from a stricture in the abdominal portion of the ureter, complicated by calcified glands in the broad ligament of the same side, the calcified glands may be confused in the film with ureteral stones. Such a strictured, calcified area is probably an acquired condition and due, as a rule, to a previous inflammatory process.

A plain roentgenogram and a urogram should be made to determine the exact location of the stone in the ureter. It is also necessary to learn from the x-ray study the dimensions and shape of the stone, whether there is dilatation or infection of the affected ureter and the associated kidney, and the function of the kidney. One should determine whether there is any congenital variation present in the patient suffering from ureteral calculus, since stenosed orifices, ureteroceles, and congenitally strictured ureters increase the difficulty of instrumental extraction of calculi.

In cases seen early, excretion urography serves admirably; but if the obstruction has been long continued, so that there has resulted serious injury to the kidney and impairment of its function, the opaque medium will not be eliminated in sufficient quantity to cast a shadow.

When retrograde pyelography can be done, it will usually be found the most accurate method of detecting ureteral stones. By its use, most stones in the ureter may be located, the amount of obstruction they are causing accurately estimated, and the extent to which the ureter and pelvis are dilated above the impacted stone well visualized.

Differential Diagnosis. Ureteral calculi often give rise to symptoms which are erroneously attributed to other organs—the gall-bladder, appendix, colon, and the pelvic organs of women especially. It is here that cystoscopy and roentgenography prove so valuable.

Prognosis. The prognosis depends upon the state of the urinary tract above the stone at the time the patient first comes under treatment. If

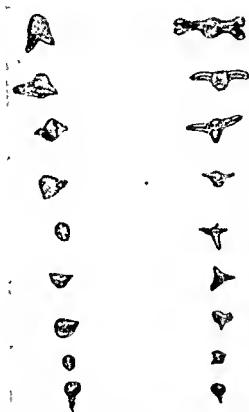


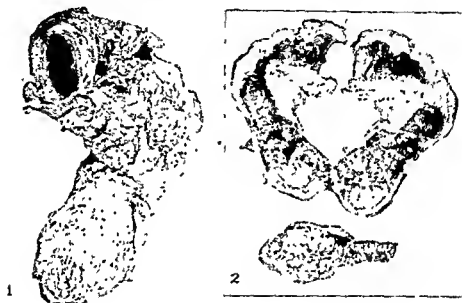
FIG. 284. Photograph of 18 stones removed from a ureter. These evidently formed in the calyces of the kidney, and sudden dilatation of the ureter and pelvis caused them to become dislodged and to pass into the dilated ureter, whence they were removed by ureterotomy.

a stone is discovered early and removed promptly, whether by open operation or by cystoscopic methods, the prognosis is regularly good. But if the function of the associated kidney is already seriously impaired, or there is pronounced hydronephrosis or pyonephrosis, or if, in addition to renal impairment, there is dilatation and permanent thickening of the ureteral wall from back pressure, stasis, and infection, the chances of saving the kidney are poor.

The prognosis should always be guarded. Recurrence is likely in any

case, irrespective of the treatment, unless the basic cause of the stone-formation can be removed. The reports vary so widely that it is impossible to estimate the average of recurrence in ureteral stone.

Treatment. Many ureteral stones will pass spontaneously, while the majority requiring treatment can be dislodged by cystoscopic maneuvers. The removal of an obstructing ureteral calculus presents the surgeon with a problem calling for the exercise of his very best judgment because of the many factors that require consideration.



tesy of Dr Alfred T Osgood)

There are no set rules for the treatment of ureteral calculus. It should be emphasized, however, that persistent and heroic measures to remove a stone cystoscopically, with too long a postponement of surgery, may be at the expense of extensive and permanent damage to the obstructed kidney or even loss of the patient's life. The following factors should be considered in determining the proper management of each case:

(1) *The size of the stone.* It is the prevailing opinion that stones larger than 1 cm. should be removed by ureterolithotomy rather than by cystoscopic manipulation. The larger the size, the less likely is it that manipulative efforts will succeed. Fortunately, the great majority of ureteral stones are of smaller size.

(2) *Location.* The position of the stone in the ureter, and the probable length of time it has remained in this position, are of first importance in the choice of treatment. A stone located in the lower third of the ureter is decidedly more amenable to manipulative removal than one lodged farther up. If the stone is located higher up, and is less than 1 cm. in diameter, expectant treatment may be employed for a few days in the hope that it may progress into the more favorable pelvic portion of the duct. Calculi more than 1 cm. in diameter, above the pelvic brim, usually require ureterolithotomy.

(3) *Duration of symptoms.* A patient under treatment for a first attack of renal colic is usually treated much more conservatively than one who gives a history of attacks occurring over a period of weeks or months. If the onset is recent, expectant treatment for a few days may be followed by the spontaneous passage of a stone.

(4) *The condition of the kidneys.* The condition of the associated kidney (the extent to which it has been affected by obstruction and infection) and the condition of the opposite kidney (its functional ability, and whether or not it shows stone or associated pathology) will influence the decision as to whether immediate surgery is necessary or it is safe to delay while attempts are made to remove the stone cystoscopically. When infection is acute and severe, in the presence of an obstructing calculus, prompt surgical interference, with the establishment of free drainage, may become a life-saving measure. Infection may become acute and spread rapidly following unsuccessful manipulative efforts, rendering surgery necessary.

(5) *The general condition of the patient.* This should be carefully weighed in connection with other factors before deciding upon the plan of treatment. Distinctly toxic patients should be handled with caution and concern. If a catheter cannot be passed, or if catheterization is not at once followed by improvement, nephrostomy should immediately be performed irrespective of the size or location of the stone.

(6) *Anuria.* Total anuria, due to obstruction of a solitary kidney or of both ureters by stone, requires immediate nephrostomy unless it is possible to negotiate the obstruction by an indwelling catheter.

The treatment of ureteral stone is: (1) symptomatic, (2) expectant, (3) instrumental, (4) surgical.

Symptomatic Treatment. There is no pain more agonizing than that of acute ureteral or renal colic, and it can be relieved only by morphine or one of its derivatives. When the pain is intense, morphine in 0.015 Gm. (0.25 gr.) doses is the drug of choice; when it is moderate, codeine in 0.06

Gm. (1 gr.) doses is advisable. If sedatives are not immediately available or are for any reason contraindicated, temporary relief will usually be obtained by putting the patient in a very hot bath. If the obstruction causes only backache, a hot water bottle or heating-pad applied to the affected loin will be comforting.

Expectant Treatment. In cases where the patient is experiencing his first attack of renal or ureteral colic, or is known to have successfully passed ureteral stones, the medical attendant is justified in using expectant treatment, which implies watchful waiting for spontaneous delivery of the stone. This should not be done unless it has been demonstrated by functional tests and pyelography that the kidney is not suffering from the effects of back pressure, and that the condition of the lower urinary tract is such that it can be depended upon to cooperate in the spontaneous expulsion of the stone. The treatment consists of forced fluids, the use of urinary antiseptics, and atropine sulphate at intervals to relax the ureteral musculature. Expectant treatment is very easily carried beyond the limits of safety to the patient, and requires that the patient be closely observed.

Instrumental Manipulation. When the size and location of the stone, and the condition of the kidneys and the patient justify it, every effort should be made to remove the stone through the cystoscope. Manipulations are not without risk, however, and the contraindications to this method will be considered in a moment.

The principles employed are dilatation, lubrication and anesthetization of the ureter, and dislodgment, grasping, or crushing of the calculus. The various types of instrumental manipulation may be divided as follows:

(1) The insertion of a ureteral catheter above the stone for the purpose of drainage, to relieve back pressure and combat infection. The catheter is left in position and in cases with markedly diminished function the degree of improvement following adequate drainage will determine the future course.

(2) Dilatation of the ureter: (a) by the insertion of an inlying ureteral catheter; (b) by passing bulbed catheters and bougies of increasing sizes; (c) by the use of multiple catheters to form a mesh, if several can be simultaneously passed behind the stone; (d) by the use of special dilators for the mechanical dilatation of the ureteral lumen and orifice. Dilatation of the ureter, and dislodgment of the stone by manipulation with the tip of the catheter or a bougie, will result in expulsion of many calculi

lodged in the lower third of the ureter. Sometimes a stone will have been lodged in a position near the vesical orifice long enough to have caused considerable dilatation of that portion of the ureter just above the impaction. If the calculus can be pushed back up the ureter into the dilated portion, catheters or bougies of increasing caliber may be introduced into the portion formerly occupied by the stone. Thus, by gradual dilatation, the lower lumen will be widened sufficiently to permit peristaltic action to push the stone through the dilated portion into the bladder.

(3) Lubrication by the injection of sterile oil or glycerine above the stone. This is usually used in conjunction with a local anesthetic, which will cause the ureteral musculature to relax.

(4) Extraction with one of the numerous special extractors, forceps, or snares. Most of these can be used with safety only in the lower third of the ureter. (The safest and most useful stone "extractor" is the ureteral catheter assisted by the instruments ordinarily used to dilate the ureter and its meatus.) When the stone presents at the ureteral orifice it is easily removed with the Lowsley or Kirwin grasping forceps.

The procedure of passing multiple catheters and leaving them in from 24 to 72 hours (first advocated by Bumpus) has at least the value of safety. The catheters should be twisted around each other in an effort to ensnare the stone. The ureter and pelvis are distended with water or oil at the time of withdrawal of the catheters.

(5) Enlargement of the ureteral orifice by cystoscopic scissors or the fulguration tip. Most low ureteral stones can be made to pass by ureteral dilatation and manipulation, provided the ureteral orifice is incised to accommodate the diameter of the stone.

(6) Crushing of the stone with the rongeur or stone forceps.

As shown above, instrumental removal is contraindicated when the stone is large, or firmly impacted, or complicated by serious renal changes due to back pressure or infection. There are certain patients who tolerate cystoscopic manipulations poorly and whose reactions to them are severe. In patients of this type operation must be done at once.

Surgical Treatment: The surgical treatment of ureteral calculus consists of (1) removal of the stone (ureterolithotomy) and (2) treatment of the renal complications arising from long-standing ureteral obstruction. These complications must be considered when surgical methods of removing ureteral calculi are carried out.

A pyonephrotic kidney or a permanent ureteral fistula may make

nephrectomy or ureteronephrectomy imperative. Many kidneys with milder degrees of pyonephrosis and less extensive destruction of tissue will return to a surprisingly good functional state once the obstruction is removed and drainage re-established. The choice between radical and conservative surgery of the hydronephrotic kidney likewise depends upon the extent of the renal impairment and the condition of the other kidney. Occasionally, total anuria or some other complication will necessitate an emergency nephrostomy with postponement of removal of the stone until the patient's condition has improved.

Ureterolithotomy should be performed when impacted calculi show no tendency to descend after expectant or manipulative treatment. Surgery is usually the only resort in cases where the stone has lodged in one spot for a long time, so that periureteral thickening and partial stricture have already occurred. If a diverticulum has formed, this must usually be resected. Cystoscopic manipulation should not be continued when evidence of increasing renal damage is apparent, or in the presence of unrelieved pyelonephritis.

The surgical removal of ureteral calculi is discussed under Operative Treatment of the Ureter (p. 1320).

After-care. An attempt to assess the etiological factors should be made in every case, in an effort to diminish recurrence by attention to the causative or predisposing factors. There is much still to be learned as to why stones form and what steps will prevent a recurrence. Evidence points, however, to stasis, infection (focal or local), metabolic disturbances such as hyperparathyroidism, and deficiency of vitamins A and D as being factors of importance. Close attention to these points will result in a reduction in recurrent renal and ureteral stone. The chemical composition of stones should be studied with the view of correcting faulty metabolism.

Obstructive Conditions of the Ureter and Ureteropelvic Junction

Under this heading there will be considered four conditions, all of which are fairly common: (1) stricture, (2) kinks and angulations, (3) hydro-ureter, (4) non-calculous obstructions of the ureteropelvic junction.

STRICTURE OF THE URETER

Stricture of the ureter, as an etiological factor in disease of the upper urinary tract, was but little regarded until 1911, when Hunner began his long series of publications regarding the etiology, pathology, and

incidence of ureteral stricture in the female. The most frequent form of stricture, according to this author, is the primary stricture, which was defined by him as a localized intrinsic inflammatory process in the wall of the ureter, metastatic in character and due to focal infection. Although his views have been widely questioned, many eminent clinicians are fully in accord with them. Whether or not one agrees with Hunner that most acquired strictures are primary, and that the urinary-tract lesions often associated with stricture (ureteral stone, hydronephrosis, pyelitis, pyonephrosis, Bright's disease) are secondary to the stricture, one is forced to admit that his work has been of great significance, if for no other reason than the attention it has attracted to a formerly neglected source of genito-urinary pathology.

Sex and Age Incidence. Sex seems to play no important part, although there is a somewhat prevalent belief that ureteral stricture is much more common in females than in males. Our experience, however, does not bear this out. Church (1927), reporting on 100 cases seen at the Brady Foundation, gave the sex incidence as: males, 65 per cent; females, 35 per cent. More recent publications place the incidence as approximately the same in both sexes.

Ureteral stricture may produce symptoms at any age; but about 75 per cent of the patients are in the third, fourth, and fifth decades of life—the fourth decade being the most common. M. F. Campbell has recently reported that postmortem studies of the urinary tract in children indicate that the ureter is congenitally obstructed in about 1 per cent, and of these obstructions congenital stricture is by far the most frequent. In his reported series of 12,080 autopsies in children, stricture occurred in 0.6 per cent. These congenital strictures are probably the chief predisposing factor in the chronic pyelitis of childhood.

Etiology. Ureteral stricture may be (1) congenital or (2) acquired.

Congenital strictures are usually exaggerations of the normal physiological points of narrowing in the ureter, unaccompanied by infection. They occur with about equal frequency in both sexes, and are often bilateral. Another congenital cause of ureteral constriction is the *ureteral valve*. Valves are transverse folds of redundant ureteral mucosa, usually about 1 cm. above the ureteral orifice. They rarely cause serious obstruction, and generally disappear during the first 6 months after birth. Woelfler found them in 20 per cent of newly born infants studied by him postmortem.

Acquired strictures are (1) non-inflammatory and (b) inflammatory.

Non-inflammatory strictures are chiefly traumatic, and may follow external trauma (rare), the injuries of labor, surgical operation (most common), careless or unwise ureteral dilatation, or erosion by a calculus. Extraureteral compression by cysts, tumors, enlarged glands, etc., may also cause constriction of the ureter. Scar tissue may surround and choke the ureter following severe parametritis or injuries sustained during labor. Aberrant vessels not infrequently compress the ureter. The duct may also be compressed from without by fibrous bands or by adhesions to adjacent organs.

Inflammatory strictures are (1) primary and (2) secondary. We are inclined toward a median position in the controversy over the frequency of primary stricture. Although stricture due to bacterial metastasis to the ureteral wall from focal infection in the teeth, tonsils, or sinuses, or from disease of the digestive tract, may not be as common as Hunner would have us believe, the assertion of Beer and his colleagues, Schreiber, and a number of others—namely, that the lesion described by Hunner either does not occur or is extremely rare as compared with stricture due to other etiological factors—seems to us contrary to the known facts. Infection may also reach the ureteral wall by way of the lymphatics, passing from below upward or through the lymphatics which anastomose with those of the colon.

Secondary inflammatory strictures are most commonly the results of extensions of infection from the adnexa or bladder, or are consequent to acute renal infection. Any of the common pyogenic or specific organisms may be responsible: streptococcus, *Staphylococcus albus*, *Bacillus coli*, gonococcus, tubercle bacillus, *Spirochaeta pallida*, etc. The intramural portion of the ureter is often narrowed as a result of tuberculous or other forms of chronic cystitis.

Pathology. About two-thirds of congenital strictures will be found at the ureterovesical junction. The majority of the remaining one-third occur at the ureteropelvic junction—congenital stricture of the body of the ureter being uncommon. Occasionally, the ureter is congenitally strictured at both ends.

Acquired stricture may occur in any portion of the ureter, but is also rather uncommon in the body of the duct. Almost as many occur in the upper as in the lower portion. Of 66 cases of ureteropelvic obstruction proved by operation, at the Brady Foundation in the New York Hospital, 31 revealed a stricture of the ureter (congenital or acquired) at its entrance into the pelvis (Henline, 1935). The stricture usually

shows connective-tissue proliferation and cicatricial contraction involving all the coats of the ureteral wall. The actual lesion may vary from a simple annular narrowing to an extensive area of dense infiltration. The involvement of the layers begins with the lining of the lumen and spreads over the mucous coat, setting up ulceration, connective-tissue proliferation, and, eventually, contraction sufficient to greatly narrow the lumen. These effects are due in part to irritation of the inflamed surface by urinary salts and in greater measure to the activities of bacterial organisms. These organisms are by no means specific, as at one time or another practically all those found in the urinary tract have been implicated as causal factors in ureteral stricture.

Hydronephrosis, in greater or less degree, occurs in a considerable proportion of the cases. Hydronephrotic destruction of the kidney may be the end result when the obstruction is not relieved. When the stricture is near the vesical end, the adjacent proximal portion of the ureter usually shows the earliest dilatation. The obstructive changes in the kidney and ureter may occur gradually and continue for long periods of time without producing symptoms sufficiently striking to direct attention to the upper urinary tract. When infection complicates the obstruction, irreparable injury to the kidney may occur. Stricture of the ureter is an important factor in the etiology of so-called essential hematuria and in the production of chronic interstitial nephritis. The etiological relationship of stricture to calculus and to the chronic pyelitis of childhood has already been emphasized.

Symptoms. The symptoms associated with stricture of the ureter are "multifarious and sometimes bizarre" (Hunner).

In children, in whom the stricture is usually congenital, the urological investigation in most instances is prompted by persistent urinary infection (Campbell, 1939). Persistent pyuria and pain in the loin are the commonest symptoms. Since cure of the infection is extremely difficult without first eradicating the obstruction, the establishment of the presence of stricture is of great importance in these fairly common cases. In the absence of infection, serious renal damage due to obstruction may give the clinical and laboratory picture of chronic interstitial nephritis.

In adult patients, the principal symptom is pain. The pain is most commonly located in the loin. In some cases pain in the loin is the only subjective symptom, and is usually directly attributable to hydronephrotic or ureteral distention due to the obstruction. Frequently, however, patients complain of lower abdominal pain and discomfort,

with or without pain in the back. Some patients complain of pain radiating down the thigh or leg, into the sacral or iliac regions, or to the region of the thorax.

Many patients have gone from physician to physician in an effort to rid themselves of the abdominal discomfort. Not infrequently symptoms due entirely to the ureter will be attributed to neighboring organs, notably the appendix, the ovaries in women, and the seminal vesicles and prostate in men. If pathological conditions do happen to exist in adjacent viscera, attention will most likely be focused upon them and the ureter entirely overlooked. If an unfruitful surgical operation has been done, the persisting symptoms will then be blamed upon "postoperative adhesions," and still further surgery may be carried out to release these supposed causes of pain and disability.

Gastrointestinal symptoms are common in both adults and children, and range from slight nausea to vomiting, gaseous distention, constipation, and rectal tenesmus.

Vesical symptoms are fairly prominent, but may be entirely lacking in some cases. Dysuria, frequency, and urgency are complained of. Intermittent pyuria is common. Hematuria frequently results from hydronephrotic distention.

Headache and nervous symptoms are frequent. If urinary infection is present, there are likely to be chills, fever, and other symptoms of generalized infection, such as are seen in appendicitis.

With advanced destruction of renal tissue (in solitary kidney or bilateral cases) urosepsis is manifested by headache, mental lassitude, stupor, and finally death from urinary toxemia.

The urine may be quite normal in many cases. In others, it contains pus, blood, albumin, and organisms.

Diagnosis. Failure to recognize and properly treat this lesion has resulted, in the past, in much chronic suffering and in innumerable unnecessary operations, due to errors of diagnosis.

The diagnosis depends upon the salient points presented by (1) the case history, (2) the ordinary physical examination, and (3) urinalysis. If these point to the possible presence of a ureteral stricture, a complete urological examination should be made. Instrumental exploration and urography should leave little doubt as to the diagnosis.

Ureteral stricture is often suggested by the history of persistent or intermittent pain along the course of the upper urinary tract, particularly if there are also gastrointestinal disturbances and bladder symp-

toms, and if urinalysis shows blood or pus. The occurrence of pus or blood in the urine is irregular. It is therefore important that a series of urine examinations be made at fairly wide intervals, since the urine may be clear at one examination and at another contain pus, blood, or organisms. In many cases, however, the urine is quite normal.

Bimanual palpation of the kidneys and ureters will be of service in revealing tenderness. In women, the ureters are easily palpable on vaginal examination, and when there is present a stricture, ureteritis, or both, palpation will usually elicit tenderness or pain at one of the following points: (1) along the upper urinary tract, (2) where the ureter crosses the pelvic brim, (3) in the duct's juxtavesical portion (the most common site of stricture). Rectal examination is also useful.

Cystoscopy will not often show marked cystitis, but in a majority of cases there will be increased vascularity about the ureteral orifice of the involved side.

For the recognition of ureteral stricture or other obstruction, the ureteral catheter, ureteral bulb, and the ureteropyelogram are essential. If the stricture is low down and dense, it may be impossible to introduce a catheter, and if it passes, but causes great pain, the presumption of stricture is much increased. Obstruction to the passage of a bulbed catheter, or the "hang" obtained at the site of obstruction on withdrawal, is presumptive of stricture, but is not definite proof since it is frequently caused by spasm.

The point of stricture can be demonstrated in most cases by retrograde pyelography. Serial pyelograms are especially useful. Excretory urography is also satisfactory, particularly in children, unless there is advance renal injury.

Differential Diagnosis. Stricture must be differentiated from other obstructive conditions of the ureter, such as hydro-ureter and kinks or angulations. For this, ureteropyelograms in the prone and upright positions are of great importance. Since the ureteral catheter may act as a "splint" which straightens out abnormal twists and angulations, after the opaque medium has been injected a picture should be taken, the catheter then withdrawn to a point below the upper limit of the bony pelvis, and another roentgenogram taken. When the ureter no longer contains anything firm enough to straighten and stiffen it, the kink or angulation will be in evidence.

Spasm simulating stricture may inject an element of confusion. When attempting to introduce a catheter into a spastic ureter, one may get

the impression that he is dealing with an impassable stricture. It must be remembered, however, that if secretion by the kidney is for any reason temporarily suspended, as occasionally happens from the psychic effect of the examination alone, the unmoistened lining mucosa of the ureter will offer effective resistance to the passage of the catheter. If the apparent obstruction is at the ureterovesical "valve," the existence of spasm should be strongly suspected. A pyelogram made after the failure of the catheter to pass often shows *nothing* obstructive at the point where its progress was halted. Sometimes, if the catheter is withdrawn, and a short interval of time allowed to elapse before it is reinserted, the secretion of urine will have resumed and the tip of the catheter passes the point where it was previously obstructed without any trouble.

Other causes of ureteral spasm that have been suggested are trabeculation of the bladder-wall musculature, syphilitic lesions of the cord, or other neuropathic causes. Fatigue and nervous exhaustion may cause it, just as these influences induce spasm at the pylorus and elsewhere. Calculi may cause irritation, or the presence of highly acid or alkaline urine in the bladder may induce secondary irritative stimuli sufficient to cause ureteral spasm. The more extended use of excretion urography will help to do away with the confusion caused by a spastic ureter, for it is the presence of the catheter carrying the opaque medium which induces spasm in most instances.

Prognosis. The prognosis of stricture of the ureter will depend on the degree of renal damage by urinary back pressure and infection. In cases seen early, and in which the stricture proves amenable to dilatation, the prognosis is usually excellent. If of long standing, so that serious injury to the kidney has taken place, the outlook depends upon what can be done to relieve and remedy the renal condition. In many cases, advanced upper urinary-tract disease, due to the obstruction or the complicating infection, will require radical surgery and frequently loss of the kidney. If the obstruction is unilateral, the sound opposite kidney may be expected to maintain life if the diseased kidney must be removed. If bilateral, the general debility consequent to the combined kidney impairment may seriously handicap recovery.

Treatment. Strictures of the ureterovesical junction, lower segment, or body of the ureter can usually be satisfactorily treated by periodic progressive dilatation with bougies. The amount of dilatation necessary, and the length of the intervals between treatments, will depend on the rapidity of dilatation and the rate of recontracture. Some patients

require only a single dilatation, or 2 or 3 treatments; while others require periodic dilatation over a long period of time. As a rule, congenital and traumatic strictures are not as amenable to dilatation as those of inflammatory origin. The dilatability of different inflammatory strictures also varies greatly, according to the virulence of the infection that produced the lesion, which influences the density of the scar tissue.

When the caliber of the strictured ureter has been ascertained, the corresponding size of ureteral bougie should first be introduced, and thereafter larger sizes in gradually ascending scale—no more than two or three being applied at any one session. Frequently, the best results follow the use of the multiple-bougie method—that is, the passing of several ureteral bougies into the ureter at the same time. This may be accomplished by using a specially constructed composite instrument.

As infection complicates many cases of ureteral stricture, in both children and adults, the instrumental treatment should be accompanied by lavage of the renal pelvis and internal medication directed at the type of infecting organism.

A congenitally stenosed ureterovesical orifice, or a resistant inflammatory stricture at this point, which does not respond to dilatation, may frequently be enlarged through the cystoscope by means of cystoscopic scissors or the fulguration point. The operation should be followed by periodic dilatation by ureteral bougies. The stenosed orifice may also be enlarged through a suprapubic cystostomy opening.

An apparent stricture of the body of the ureter, resulting from extra-ureteral pressure, can usually be satisfactorily treated by ureterolysis.

Stricture of the ureteropelvic junction is discussed further on.

KINKS AND ANGULATIONS OF THE URETER

Kinks or sharp curves of the ureter may occur in any part of the duct, but are most common in the upper third, just below the ureteropelvic junction. They are much more common in females than in males, and involve the right side more often than the left.

Etiology. Ureteral kinks may be either *congenital* or *acquired*. The ureter may be kinked at birth because of abnormal length, or because the kidney which it drains has not rotated to its proper height, or because an anomalous vessel forces it to bend out of its normal course. The anomalous vessel may not at first exert undue pressure upon a normal ureter, but later, as the size of all the viscera increases, the abnormal vessel will induce kinking. Peritoneal adhesions may likewise cause the

ureter to bend, twist, or assume a hizarre shape; and any retroperitoneal tumor mass or inflammatory process which is so located as to come in contact with the ureter may have a like effect. The most commonly recognized cause of ureteral kinking is ptosis of the kidney, but it is our belief that, actually, kinks so induced are transitory and are not nearly so productive of symptoms as is generally supposed.

Ureteral kinks and angularities are frequently observed secondary to lower urinary-tract obstruction or obstruction of the lower ureter itself. These may continue to cause obstruction after the removal of the primary cause below. Sometimes secondary periureteritis firmly binds down the kink, producing a sharp angulation.

Experimental occlusions of the ureter (Vermooten) have shown that partial stricture of the ureter may cause marked dilatation and elongation of the duct, so that it kinks easily. Therapeutic dilatation will usually diminish or eliminate the kink. Many patients who have undergone nephropexy still suffer pain which, preoperatively, had been attributed to kinking of the ureter. Even when a renal ptosis can be demonstrated, there may be a co-existent ureteral stricture, inducing elongation of the ureter. Vermooten suggests that before doing nephropexy for the purpose of straightening out the ureteral kink it would be wise to see if relief of symptoms cannot be afforded by a course of ureteral dilatations. If urography shows that the ureter is elongated, it should be considered a possible indication of some sort of ureteral obstruction—spasm, increased physiological narrowing, or actual stricture. We have no very definite standard as to what constitutes a "normal" ureteral lumen. Very slight constriction at any point may lead to slight dilatation which may be abnormal for that particular patient. The institution of better drainage, which systematic ureteral dilatation would promote, would therefore seem a logical treatment for some of the kinks and tortuosities which now are being treated by nephropexy—frequently without relief of symptoms.

Symptoms. The symptoms are those common to stricture, stone, tumor, or other ureteral obstruction. One of the chief causes of the exquisitely painful syndrome known as "Dietl's crisis" is the kinking of the ureter which attends downward displacement of its attached kidney (Nephroptosis, p. 1624). Unless one is dealing with a genuine Dietl's crisis, however, the symptoms are not likely to be of the acute type. The patient is much more apt to complain of a dull ache in the loin, which has usually existed for some time. Many of the victims of

these kinks are regarded as *neurasthenics*, and are not infrequently subjected to gynecological procedures, such as curettage or even amputation of the cervix, because of some coincident but wholly unrelated genital-tract pathology. Occasionally, typical renal colic will supervene upon a long-standing "backache," or some other manifestation will direct the consulted physician's attention to the ureter and renal pelvis.

Diagnosis. Kinks and angulations can only be demonstrated by urography. Before the advent of urography, ureteral kinks were found only at operation or autopsy. When doing retrograde pyelo-ureterography, it is important, before taking the final picture, that the catheters be withdrawn to the lower ureter and the patient placed in the upright position. Serial pyelograms are very useful in making the diagnosis.

Treatment. When the kink is secondary to lower ureteral obstruction, ureteral dilatation will usually diminish or eliminate the angulation unless the dilatation and elongation of the ureter responsible for the kinking are considerable, or the loops are matted together by adhesions.

Restoring a ptosed kidney to its normal position by means of a properly fitted kidney belt or by nephropexy, results in straightening out of the ureter unless the nephroptosis is accompanied by enteroptosis, when the prognosis is much less favorable. With elimination of the kink, proper drainage of the kidney is restored.

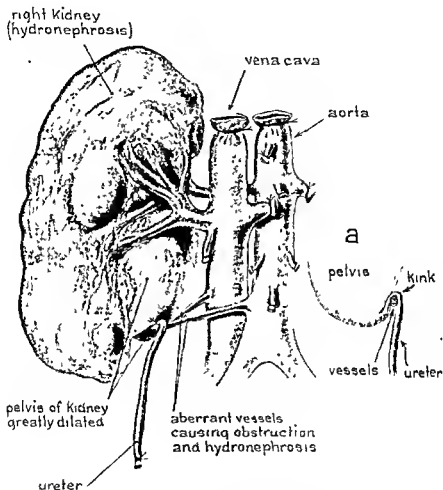
Aberrant vessels, fibrous bands, or adhesions causing or helping to cause kinking of the ureter require surgical severance (see *Surgical Treatment of Non-calculous Obstructions at the Ureteropelvic Junction* p. 1305).

NON-CALCULOUS OBSTRUCTIONS OF THE URETEROPELVIC JUNCTION

Congenital and acquired abnormalities of the ureteropelvic junction are quite common in both young and adult subjects of both sexes. They are of many different types, but have one feature in common, namely, they cause obstruction of the ureteropelvic junction, with resultant dilatation of the renal pelvis and calyces. The stasis predisposes to infection, with the production of peripelvic adhesions and fibrosis, thus increasing the pressure on the ureter. If the obstruction is not relieved, hydronephrotic atrophy and, eventually, total destruction of the kidney will result.

Causes of Obstruction at the Ureteropelvic Junction. Ureteropelvic obstructions may be due to one or more of several different factors, either congenital or acquired: (1) *true stenosis*, (2) *high insertion of the ureter in the renal pelvis, with valve effect*, (3) *extraureteral compression by an*

anomalous renal blood vessel, (4) horizontal axial rotation of the kidney (5) nephroptosis, causing kinking of the ureter. Usually, more than one etiological factor is involved.



Wm P Didusch 1931

FIG 286. Postmortem specimen showing hydronephrosis due to aberrant artery and vein to the lower pole of the kidney. The insert (a) shows the aberrant vessels on section and the kinking of the ureter.

Anomalous Renal Blood Vessels. Anomalous renal blood vessels have long been regarded as the most frequent cause of obstruction at the ureteropelvic junction. While they are undoubtedly the primary and sole cause in some instances, much more often such aberrant vessels act in

conjunction with other factors (stenosis, abnormal insertion of the ureter, excessive mobility or ptosis of the kidney) to impede drainage from the renal pelvis. Stenosis is a frequent primary cause of ureteropelvic obstruction, and when it occurs in association with an aberrant vessel the stenosis may readily be overlooked, so that treatment will be directed only to the secondary but more obvious cause of the obstruction, with the result that symptoms persist.

Regarding the incidence of anomalous renal blood vessels in association with ureteropelvic obstructions, Mayo, Braasch and MacCarty (1909) reported 27 cases of ureteropelvic obstruction, in 20 of which aberrant vessels were found. Of 66 cases of ureteropelvic obstruction reported on by Henlioc (1935) aberrant vessels were found in 29. Figures published from the urological clinic of The Johns Hopkins University Hospital show that in more than 4,000 routine roentgenological examinations there were found 528 cases of hydronephrosis, 113 (21.4 per cent) of which showed definite evidence of obstruction at the ureteropelvic junction; of these, 61 were diagnosed as being due to aberrant blood-vessel obstruction, the diagnosis being subsequently confirmed at operation.

Just how these misplaced and supernumerary blood vessels act to induce the pathological changes seen at operation and autopsy is not clearly comprehended. Some observers—notably Quinby—claim that the peristaltic action of the ureter may be interfered with by the aberrant vessel “causing sufficient interruption of these waves, through the years following birth, to bring about the resulting dilatation of the pelvis.” If fibrosis is set up about the meeting-place of the ureter and aberrant vessel, or a fibrotic condition is induced by renal ptosis in conjunction with an anomalous artery or vein, compression of the ureteropelvic junction by the blood vessel would be highly probable. If this assumption is correct, obstruction should be seen often at the point where the ureter crosses either the terminal portion of the common iliac vessels or the beginning of the external iliac vessels. However, as a matter of clinical observation, it is exceptional to find obstruction at either of these points.

Moore is of the opinion that aberrant vessels may, as the individual develops, acquire a relationship to the ureter abnormal enough to produce obstruction and hydronephrosis, because, although such vessels are often found when exploring hydronephrosis in adults, they are practically never observed in the hydronephrosis of childhood. He is inclined to lay the blame upon abnormal renal mobility. When the patient is erect.

and the kidney making its normal excursions during respiration, "the frequent impingements of the organ over an unyielding vessel may eventually lead to dilatation of the pelvis, accompanied by increase in weight, and, finally, to angulation of the ureter with actual mechanical obstruction." This view is compatible with the finding of hydronephrosis associated with aberrant vessels in the third and fourth decades of life.

Another possible inducement to pathological conditions because of the existence of aberrant renal vessels is a lateral insertion of the ureter, with the formation of a valvular type of obstruction. If interference with adequate pelvic drainage occurs—from compression of an anomalous vessel or otherwise—pyelectasis will be induced. As the sac increases in size, more compression is exerted on the ureter. The stasis predisposes to infection, with the production of peripelvic adhesions and fibrosis, as has already been mentioned.

The pathological picture is, indeed, so infinitely variable that no description of it can be given which will even approximately fit all cases. All renal surgeons know that anomalous vessels frequently exist without causing the slightest obstruction. It is our opinion that while vascular anomalies are undoubtedly the primary cause of ureteral obstruction in some instances, much more often they play a secondary role.

Stenosis. Stenosis appears to be the most common *primary* cause of obstruction at the ureteropelvic junction. Of 66 cases of ureteropelvic obstruction proved by operation at the Brady Foundation, of the New York Hospital, 31 showed stenosis of the ureter at its entrance into the renal pelvis (Henline, 1935). In a later series of 14 cases (4 of them bilateral) treated by operation at the Brady Foundation, stenosis, alone or in association with other obstructive factors, was found to be present in 15 ureters, and was regarded as the primary cause of obstruction in every case (Henline and Menning, 1943). The stenosis may be (1) congenital smallness of the lumen, without pathological tissue change, or (2) acquired, and due, as a rule, to inflammation. It may be the sole cause of obstruction, or it may be associated with other obstructive conditions, especially high insertion of the ureter, or an anomalous vessel.

High Insertion of the Ureter. High insertion of the ureter on the renal pelvis, with or without stenosis, vascular anomaly, or other abnormality, is another fairly common cause of obstruction at the ureteropelvic junction.

Symptoms and Diagnosis. The symptoms are those common to all

ureteral obstructions, and the diagnosis is dependent upon the findings of retrograde pyelography, including serial pyelograms, which are particularly helpful in demonstrating delayed emptying of the renal pelvis. When the obstruction is of such a nature as to produce periodic attacks of severe pain, or even a typical Dietl's crisis, the affected kidney may be palpable; but much more common is pain in the flank, which may be intermittent or continuous, but, while distressing, is not extremely severe. Accompanying this are gastrointestinal disturbances and symptoms of recurrent acute infection of the urinary tract, such as fever, urinary frequency, dysuria, pyuria, etc.

While pyelograms are invaluable for demonstrating the presence of obstruction at the ureteropelvic junction, one usually cannot by this means determine the nature of the obstruction. Often this cannot be ascertained except at the operating table.

The "squaring off" appearance of the under border of the kidney, which Waters found to be present in compression of the ureter by an anomalous vessel even before hydronephrosis can be demonstrated, he offers as an early diagnostic sign obtainable by roentgenography. It gives the renal pelvis an appearance similar to that of an inverted bag to one end of which a string has been tied. A later sign is dilatation of the renal pelvis, followed by hydronephrosis. When this has taken place, the pelvis has a tendency to sag over a fixed point—the ureteropelvic junction—and the "squaring off" picture becomes much more evident. This picture is quite different from that witnessed when the dilatation is produced by stones or other obstructive agents located further down in the urogenital canal.

Treatment. Obstructions of the ureteropelvic junction do not as a rule respond satisfactorily to ureteral dilatation. Some form of surgery is usually required (see *Surgical Treatment of Non-calculous Obstructions at the Ureteropelvic Junction*, p. 1305).

HYDRO-URETER

Dilatation of the ureter may be due to mechanical obstruction, or it may occur without obstruction. The non-obstructive types may be congenital, or of intrinsic inflammatory origin, or due to loss of muscular tone resulting from disturbances of innervation. These are discussed separately (*Dilatation of the Ureter Without Obstruction*, p. 1291).

Dilatation, elongation, and tortuosity of the ureter due to mechanical obstruction is a relatively common condition not only in adults but also in children and even infants.

Etiology. The causes of ureteral obstruction have been discussed under preceding headings. They may be briefly summed up as: (1) obstruction of the ureteral lumen by inflammatory reaction and scar tissue, calculi, new growths, or, rarely, an organized blood clot; (2) pressure from extraureteral causes, such as tumors or edema in neighboring organs, aberrant blood vessels, adhesions and fibrous bands attaching the ureter to other structures; (3) congenital malformations, valves, folds, kinks and angulations, and, in particular, stenosis of the ureter's lower end; (4) acquired kinks (in connection with movable kidney), twists, and angulations; (5) injury of the ureter due to trauma or surgery. Any of these obstructions, if unrelieved, may serve to induce hydro-ureter.

Obstructions of the lower tract eventually have the same effect upon the ureter as obstructions of the duct itself. Thus, we often see acquired hydro-ureter in advanced cases of prostatic hypertrophy which have been left untreated or have been improperly handled. Angulated hydro-ureters are particularly common in obstructions of the lower tract in children—notably congenital valves of the posterior urethra. The dilated, elongated ureters form loops or coils, which become fixed through the formation of fibrous and connective-tissue adhesions. Removal of the primary obstruction in the posterior urethra will fail to halt the renal destruction, because these adherent loops act as secondary valves to maintain or increase the obstruction. Resection of a portion of the angulated, elongated ureter has occasionally resulted in straightening out of the kinks of the remaining portion and the restoration of fairly good drainage to the kidney.

The obstruction most frequently met with in childhood is stenosis of the ureter. When the entire ureter is dilated, the stenosis will be found at the extreme lower end, where the ureter enters the fundus of the bladder. Normally, the ureter traverses about 2 cm. of the bladder wall in an oblique direction before opening into the interior. When stenosis exists, the ureteral lumen is reduced in size to little more than a straw's breadth. Sometimes the lumen is completely blocked, but in cases where this has been found *postmortem*, there have usually been inflammatory changes present, so that the narrowed lumen was still further reduced or completely obliterated by the edema. It is generally accepted that stenosis of the ureter, whether at the upper or lower end, or where it crosses the brim of the pelvis, is due to some developmental fault, and is, therefore, of congenital origin.

Pathology. If the primary obstruction is in the ureter, there will be

dilatation and distortion of the duct above the site of blockage, with more or less associated hydronephrosis or atrophy of the corresponding kidney, depending upon the degree and duration of the obstruction. If the obstruction is in the lower urinary tract, there will usually be dilatation of the entire ureter and the condition will, as a rule, be bilateral. Rarely, the ureter immediately above the bladder dilates, without distention of the renal pelvis and kidney.

The ureter is often tremendously dilated and elongated, with walls many times their normal thickness. In Culver and Baker's case the hugely distended ureter was 42 cm. long, markedly tortuous and thick-walled. At the bladder end the outside diameter was about 3 cm., while just below the ureteropelvic junction it was 1.5 cm. The convolutions may be matted together by adhesions. Experimentally, hydro-ureters of enormous proportions have been produced by Hosford and Gruber.

Symptoms and Diagnosis. Early in life the symptoms are those of urinary obstruction; later on, they will be those of obstruction and infection. A child suffering from urinary-tract disturbances, such as dysuria, frequency, urgency, dribbling or complete incontinence, or frank retention, should be suspected of possessing "congenital" hydro-ureter or hydronephrosis. Pus in the urine, especially in little boys, should always arouse suspicion and demand an immediate investigation. When infection ensues, the colon bacillus will be found to be the most frequent invader.

The diagnosis has already been discussed under obstructions of the ureter. Rectal examination should always be undertaken, for without it, much suggestive symptomatology may be overlooked. Renal function tests, estimation of blood urea, and the other measures which give information concerning the functional and anatomical states of the whole upper urinary tract, must always be brought into service.

Treatment. The various means of dealing with hydro-ureter are mentioned in connection with the different forms of ureteral and lower-tract obstructions responsible for the condition.

Ureterocele

Ureterocele (cystic dilatation of the lower end of the ureter; intravesical ballooning of the ureterovesical septum; intravesical cyst), while formerly considered a very rare lesion, which was diagnosed usually at the autopsy table, has been discovered with ever-increasing frequency with the wider employment of cystoscopy and roentgenographic visualization of the

urinary tract. Rhodes (1936) reports seeing 13 cases in 695 cystoscopies—an incidence of almost 2 per cent.

It is important to distinguish between ureterocele and prolapse of the ureter (p. 1290). In prolapse, there is an extrusion of the ureteral mucosa, either alone or with all the layers of the ureteral wall, so that the extrusion is covered on its vesical aspect by ureteral mucosa. In ureterocele, all the layers of the ureteral wall are involved in the intravesical protrusion, but with no alteration in their normal relations; that is, the vesical aspect is covered by bladder mucosa and the inner aspect by ureteral mucosa, with fibrous tissue between the two mucous layers. Failure on the part of many writers to distinguish between these two conditions has led to many erroneous conclusions.

Etiology. It is generally agreed that the ballooning is due to narrowing of the ureteral meatus as a result of either congenital or acquired conditions. Some authors believe that the stenosis is always congenital. Another group suggests as possible etiological factors inflammatory changes about the ureteral orifice, due to infection within the bladder or in the pelvis, and trauma due to instrumentation or the passage of stones. The literature on the etiology of ureterocele was well reviewed by O'Connor and Johnson (1930), who found a wide variation of opinion and considerable embryological and clinical evidence to back up almost any viewpoint.

Factors favoring a congenital defect are (1) the comparative frequency with which ureterocele is found in infants and young children, (2) its frequent association with anomalous conditions of the upper urinary tract, particularly supernumerary ureters, (Fig. 276), (3) the tendency to bilateral involvement.

In favor of an acquired origin is the common occurrence, at all ages, of cystitis, which may eventuate in stricture of the ureteral orifice due to the presence of scar tissue. Hunner also mentions the possible influence of focal infections in the development of this condition. Petillo holds that obstruction in the lower ureter (which may be caused by attachment of a seminal vesicle in the male, or an adhesion to the broad ligament in the female) causes paralysis of the intramural portion with loss of contractile power, and continuous pressure from above results in dilatation of this atonic portion and intravesical protrusion. Papin looks upon ureterocele as merely the lower segment of a hydro-ureter, which must of necessity be preceded by stenosis of the ureteral orifice.

Landwüst regards ureterocele as a widening within the bladder cavity

of the terminal portion of the ureter, which can occur only when a stricture is present in conjunction with an abnormally long submucosal course of the ureter's vesical end. Blum also regards a long and winding course beneath the vesical mucosa as essential to the formation of ureterocele. The theory of Böstrom assumes an abnormally oblique course of the ureter through the bladder wall.

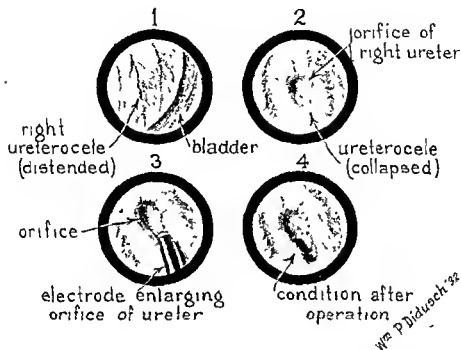


FIG. 287. Ureterocele. Cystoscopic fulguration of ureteral orifice. (1) Shows ureterocele distended. (2) Ureterocele in collapsed state. (3) Enlarging the ureteral orifice by means of the electrode, thereby permitting adequate drainage. (4) Showing the condition of the ureteral orifice after operation. (Case of Dr. Peter Lavalle.)

The weight of evidence indicates that ureterocele is dependent upon congenital stenosis of the ureteral orifice with congenital weakening of the connective tissue and muscular elements about the meatus, and that it is often aggravated by infection and trauma.

Pathology. Ureteroceles may vary widely in form and size. They may be round, elongated, or flat; open or closed; very small or of great size. In infants they have sometimes filled the entire bladder. The simplest and most common form is a small or moderate-sized balloon-

like protrusion during the ejaculation of urine, the ureteral orifice usually being located at the tip. This form may occur at any age.

Pathologically, ureteroceles are important because they serve to obstruct free drainage from the ureter and thus predispose to general infection of the urinary system, particularly the upper portion of the tract. If left untreated in its earlier stages, it may lead to hydro-ureter and hydronephrosis, or even to complete destruction of the kidney.

In cystic dilatation, there are primary and secondary changes. Whether congenital or acquired, at the outset there is contraction of the ureteral orifice. As a result of this narrowing, the upper portions of the duct are dilated by urine, and the ureter then becomes cystic and dilates intravesically. The wall of the cyst is formed by a thinning-out of the intramural portion of the ureteral wall. As the dilatation and swelling increase, the end of the ureter may descend into the urethra and (in the female) finally present in the vulva.

The cyst wall consists of two mucous layers—ureteral and vesical—which are continuous at the stenosed orifice. Fibrous stroma separates the mucous layers. The stenosed orifice will be displaced from its normal position and will usually be found surmounting the cyst.

The secondary changes are those due to obstruction, stasis, and infection.

Gutierrez has classified the more common varieties of ureterocele into six types: (1) simple unilateral ureterocele, (2) simple bilateral ureterocele, (3) ureterocele ballooning inside the bladder and containing a stone, (4) ureterocele prolapsing through the urethra and protruding beyond the meatus (more common in females), (5) ureterocele with hydro-ureter and hydronephrosis, (6) ureterocele in an anomalous condition of the upper urinary tract, in which two ureters open at the level of the ureterocele, producing hydro-ureter and hydronephrosis in a case of double kidney and ureter. In addition, he mentions three rare types: (1) *ureterocele opening into a diverticulum of the bladder*, (2) *blind ureter forming a ureterocele*, (3) *a fused type, or megalo-ureteroceles*.

Ureterocele is slightly more common in women than in men. No age is exempt. The condition has been observed in still-born infants and in the aged. Most of the patients are between the ages of 20 and 55 years. Bilateral involvement is relatively common. When only one side is affected, it is more frequently the left.

Symptoms. Symptoms are mainly attributable to obstruction and infection. The stenosis being incomplete, secondary changes in the

upper tract take place slowly. Ureteroceles therefore probably exists in some cases for years without symptoms of any kind.

The early symptoms are due to interference with the renal drainage by reason of the narrowed orifice, and are not characteristic. Dull, aching pains along the urinary tract, or pains referred to the abdomen, pelvis, or hip, are common complaints. With the onset of infection, there may be frequency, dysuria, pyuria, hematuria, and the general symptoms arising from the toxic effects of stasis—headache, gastrointestinal disturbances, and, sometimes, chills and fever.

Cysts of large size, by blocking the bladder outlet during micturition, may cause hesitancy, dribbling, or sudden stoppage of the urinary stream. Still later the cyst may prolapse into the urethra, when there is likely to be a history of incontinence.

Diagnosis. Ureterocoele can be diagnosed on the history and physical examination only in the very rare cases where the cyst, with the ureteral orifice, has prolapsed to the outside.

In other cases, the diagnosis is definitely made by cystoscopy, and usually is not difficult, especially if the cyst is large and distended (Plate VI). The more common smaller ureteroceles, with less stenosis, may be seen to fill and empty with each peristaltic wave. The ureteral orifice may surmount the ballooning area, or it may occupy a position near the base, and may not be observable until a fine stream of urine issues from it at the end of a peristaltic wave. In the larger ureteroceles, especially those with thickened walls, the cyst will have the appearance of a smooth, soft tumor which pulsates with peristalsis but does not collapse. Urine is seldom seen spurting from the contracted orifice, which is likely to be much displaced.

Intravenous urograms will clearly demonstrate the lesion in most cases. The suggestive findings by urography are: a dilated ureter narrowed at its point of passage through the bladder wall, with a bulbous dilatation of the vesical end of the ureter. Occasionally, it may be possible to catheterize the ureters, but often this will be impossible.

Treatment. The object of treatment is the restoration of good drainage for the kidney. This demands an orifice of sufficient size for the free passage of urine and the preservation of the valve-like action of the ureteral os to prevent urinary reflux.

If the ureteral orifice can be identified, simple gradual dilatation may suffice, provided the dilatation is ample enough to insure the dilated orifice remaining permanently open

Most authors recommend transurethral treatment by means of the diathermy current as a method that is generally satisfactory regardless of the size of the cyst, and that is followed, as a rule, by a rapid and uneventful recovery. This may consist of either (1) simple fulguration of the ureteral orifice with a point electrode, or (2) ureteral meatotomy carried out by means of minute cystoscopic scissors or by a knife electrode. Great care must be taken not to destroy too much of the ureterovesical valve, or urinary reflux will take place.

If the ureterocele has prolapsed to the vulva, resection of the strangulated portion is usually necessary.

Suprapubic cystotomy and excision of the cyst, by cold instruments or by the various cauterizing or fulgurating instruments, is usually reserved for ureteroceles of very large size. Excision of the cyst is often attended with ureteral reflux and pyelonephritis, and is rarely required.

Nephrectomy may be necessary in cases with markedly impaired kidney function, especially if infection is present; but in view of the remarkable recuperative power of some infected kidneys under conditions of restored drainage, it need hardly be emphasized that nephrectomy should not be too hurriedly performed. However, in ureteroceles of long standing, obstruction has frequently resulted in such marked hydro-ureteronephrosis that removal of the kidney and ureter becomes necessary.

Regardless of the method employed for opening the ureterocele, the patient should be observed from time to time until it is certain that the restored ureteral orifice remains freely open and that strictured areas higher up, if present, are well dilated.

Prolapse of the Ureter

A very rare condition, associated usually with the passage of stones, is prolapse of the vesical end of the ureter. This is confused by many earlier writers with ureterocele.

Prolapse may be due to overviolent contractions of the ureter, which, however, would have to be dependent upon some structural weakness in the ureteral wall. The previous existence of stricture with subsequent dilatation, or of calculus with resulting trauma and stretching of the ureteral wall, might result in conditions favoring prolapse of the ureteral mucosa. Redundancy of the ureter, which is sometimes put forward as a cause of kinks and twists of non-pathological origin, might predispose to prolapse.

Treatment. As a rule, the condition causes no symptoms and is only discovered on routine cystoscopic examination. It may occasionally be necessary to treat it in the same manner as the prolapsed female urethra is handled, namely, by resection of the prolapsing portion and enlargement of the ureteral orifice, if this is deemed necessary. Great care must be taken not to damage the ureterovesical "valve."

Dilatation of the Ureter Without Obstruction (Megalo-Ureter: Atony of the Ureter)

The term *megalo-ureter* was coined by Caulk to fit a single case of what was probably a primary anatomical defect in the ureteral wall, resulting in enormous dilatation of the ureteral lumen. The term has, however, been taken up by the medical profession and rather loosely applied to those conditions, congenital or acquired, in which there is permanent gapping of the ureterovesical orifice with a gigantic ureter—"permanent dilatation of the ureteral orifice" the French have termed it, because no stricture, impacted calculus, or other obstruction can be found to account for it. The condition is such that were we to turn these patients upside down when their bladders are full, the urine would flow back to the kidneys just as readily as it passes from the kidneys to the bladder when the patient is in his normal, upright position.

Etiology. Congenital megalo-ureter, or congenital idiopathic dilatation of the ureter, as it is frequently called, was first reported by Saintu in 1896 in a fetus. Many cases have been recorded since, both in the newborn and in children.

Up to the fifth month of fetal life, the ureter is of enormous caliber as compared with the rest of the body. It has been suggested that megalo-ureter is due to one of the following: (1) absence of the normal inhibition of growth at the fifth month of fetal life, so that the fetal condition of ureteral enlargement persists; (2) hypoplasia of the musculature; (3) a disturbed or deficient nervous mechanism controlling function.

Insufficiency of the ureteral orifice, which permits reflux of urine with contractions of the bladder, is a cause of ureteral dilatation. Incompetence of the ureterovesical "valve" may be the end-result of a number of different conditions, and is the forerunner of most of the cases of acquired megalo-ureter. Inflammation in the region of the ureterovesical "valve" may render that delicate mechanism functionally incompetent, so that dilatation of the ureter gradually occurs; and these cases, when later they come to examination, are likely to be considered of congenital

origin. Ureteritis without obstruction is regarded as an important factor in the production of atonic, dilated ureters.

Many observers have noted this close relation between megalo-ureter and infection. When the infection originates in the kidney, it is apparently the upper portion of the ureter which first becomes involved in the inflammatory process, on account of which it becomes dilated. The dilatation gradually involves the remainder of the ureter, the lower portion being the last to be affected. Thus, the intramural portion and the ureterovesical "valve" retain their caliber for some time. This normal-calibered portion, while previously sufficient to provide adequate drainage for a ureter which was normal throughout, now becomes inadequate when the duct above has lost its muscular tone and, therefore, its normal peristaltic action. The tightness and narrowness of the lower section, compared to the relaxed and dilated upper portion, greatly impedes drainage, and the imperfect peristalsis of the duct above adds to the inefficiency of emptying. Thus, retention of urine in the ureter is fostered, and this, in turn, increases the existing dilatation. The assumption of such a vicious circle of events would account for the frequent finding, in patients suffering from pyelonephritis, of ureteral orifices of normal size and appearance admitting to dilated and atonic ureters.

It would seem, therefore, that megalo-ureter—permanent gaping of the ureteral orifice, with a greatly dilated ureter—must be of vesical, rather than renal, origin. The findings of numerous investigators bear out this conclusion.

Disturbances of innervation explain some cases of atonic dilated ureters. The neurogenic disturbance may be the result of a congenital defect in the neuromuscular structure of the ureter itself, or of trauma or disease (as in tabes). Hydronephrosis, with dilatation of the ureter, is the inevitable result of ureteral atony.

Symptoms and Diagnosis. A considerable degree of ureteral dilatation may exist without producing any symptoms. Symptoms attributable to the condition *per se* are negligible, even in severe cases. When the bladder is distended, there may be a feeling of weight and discomfort, but seldom actual pain, in the lumbar region. This discomfort is usually felt as the bladder is being emptied. Distention of the bladder by cystoscopic fluid often produces it. The patient may have been so little troubled by these symptoms that only close questioning will elicit the history. More often, however, the symptoms due to back pressure or secondary infection will be severe enough to cause the patient to seek medical aid.

The chief characteristics of megalo-ureter are: (1) the great size of the ureteral orifice, which is gaping and rigid; (2) the complete and wide communication between the bladder and the renal pelvis.

Cystoscopic inspection will generally show a gaping ureteral orifice on one or both sides. In unilateral cases, there will be a striking difference between the normal orifice and that of the dilated ureter. Instead of a tiny slit in the wall, emitting at regular intervals spurts of clear urine, there will be seen a round hole—"golf-hall orifice" it has been termed because of its size and shape.

In some cases of atonic dilated ureters the alterations in the cystoscopic appearance of the ureteral orifice will be so trifling as to make diagnosis difficult. Atony may be suspected, however, if there is even a slight suggestion of rigidity.

Urography will confirm the diagnosis of megalo-ureter. When cystographic examination is made, complete filling of the upper tract will be observed.

Megalo-ureter must be differentiated from the common group of ureteral dilatations due to mechanical obstructions of the ureter, ureterovesical orifice, or lower tract.

Prognosis and Treatment. Megalo-ureter, when bilateral, is a very serious condition for which nothing can be done except to treat secondary infections and obstructions. The patient's life will be limited by the length of time necessary for destruction of both kidneys.

In the congenital cases, where one side is normal, anatomically and functionally, the most satisfactory course, in the opinion of most writers, is removal of the kidney and ureter of the affected side.

In some of the acquired unilateral cases, treatment may not be required. In others, dilatation of the ureteral orifice and lavage may be necessary for secondary infection. When there is advanced unilateral destruction, removal of the kidney and ureter may be required.

Transplantation of the ureter to another part of the bladder is sometimes indicated.

Affections of the Ureter in Children

Abnormal conditions affecting the ureters of children are dependent, as a rule, upon congenital malformations, which are fairly common in the upper urinary tract. In the foregoing pages we have discussed in considerable detail the pathological conditions which arise in infancy and early childhood as a result of congenitally malformed ureters.

Among the more frequently encountered ureteral abnormalities of childhood are *ureteroceles*, *congenital stenosis*, *megalo-ureter*, and *hydro-ureter* consequent to posterior urethral valves or ureteral stenosis. *Diverticulum* and *kinks*, *twists*, and *dilatations* secondary to compression from various causes—aberrant renal blood vessels in particular—may occur in children as well as in adults. Primary infection of the ureter, relatively rare in adults, is still more uncommon in early life. Nevertheless, it does occur, as do also *ureteral calculi* and *neoplasms*.

Differential Diagnosis. In children, as in older people, obstructions and infections of the right ureter frequently induce pain in the right lower quadrant and other symptoms which simulate those of appendicitis. With the especially designed instruments for use upon children, which are now available, the exact diagnostic methods of the urologist can be applied to even the youngest of patients, so that there is little excuse for mistakes in diagnosis. Although there may well be circumstances where such preliminaries must be dispensed with, generally speaking no child's abdomen should be hurriedly opened before he has been subjected to a complete urological examination.

BIBLIOGRAPHY

- AFIFI, M. A. Roentgenographic manifestations of urinary bilharziasis and calculous formations in Egypt, and intravenous pyelography. *Am. J. Roent.*, 31: 208, 1934.
- ALYEA, E. P. Cystoscopic removal of large ureteral calculi. *J. Urol.*, 40: 83, 1938.
- ASCHNER, P. W. Primary tumors of the ureter. *Surg. Gynec. & Obst.*, 35: 749, 1922.
- ASCHOFF, L. Ein bestrag zur normalen und pathologischen anatomie der schleimhaut der harnwege und ihrer drusigen anhang. *Virchow's Arch. f. path. Anat.*, 138: 119, 1894.
- BALDY, J. M. A case of surgical injury to the ureter. *Am. J. Obst.*, 33: 362, 1896.
- BARNEY, J. D. Observations on the kinks of the ureters. *J. Urol.*, 9: 81, 1923.
- BARNEY, J. D. A point in the clinical diagnosis of ureteral calculus. *Ann. Surg.*, 107: 636, 1938.
- BARNEY, J. D., and SULKOWITCH, H. W.: Progress in the management of urinary calculi. *J. Urol.*, 37: 746, 1937.
- BARTINA, J.. Some considerations on insufficiency of the ureterovesical valve. *Urol. & Cutan. Rev.*, 39: 167, 1935.
- BERGENDAHL, S. The clinical study of malignant tumors of the ureter. An operative case of ureteral sarcoma. *Acta. chir. Scandinav.*, 74: 179, 1934.
- BIANCHI, F.: Un caso ureterite con follicoli cistici. *Arch. ital. di Urol.*, 14: 179, 1937.
- BIEBERBACH, W. E., et al.: Pyeloureteritis cystica, with report of case. *Am. J. Roent.*, 31: 778, 1934.
- BLANC, H., and BOURLAND, A.: Considerations sur la pathogénie des hydronephroses par vaisseaux anormaux du rein. *J. d'uro.*, 40: 23, 1935.
- BLANCATO, G.: Sur la pathogénie de la tuberculose ascendante dans l'urétére du rein restant, après nephrectomie pour bacillose. *Arc. h. d. mal. d. reins*, 10: 376, 1936.
- BLAND, P. B.: Quoted by Reiner.

- BLOCH, J. C., AND JOMAIN, J.: Les blessures de l'urètre au cours des opérations gynécologiques. *Rev. méd. franc.*, 17: 491, 1936.
- BOBBIT, RAY M.: Extrinsic causes of hydronephrosis. *J. Urol.*, 38: 562, 1937.
- BRAASCH, W. F., AND HURLEY, M. V.: Granulomas in the urinary tract. *J. Urol.*, 18: 595, 1927.
- BRAY, J. L.: Hydronephrosis in children: 2 cases. *Am. J. Surg.*, 43: 147, January 1939.
- BREINIZER, A. G.: Injuries to the ureter as complications of general abdominal surgery. *Southern Surg.*, 6: 405, 1937.
- BROWN, ALFRED: Ureteral diverticula. *West. J. Surg.*, 44: 270, 1936.
- BRUNN, A. VON: Ueber drüsenähnliche bildungen in der schleimhaut des nierenbeckens des ureters und der harnblase beim menschen. *Arch. f. mikr. Anat.*, 41: 294, 1893.
- RUGBEE, H. G.: Diverticulum of the ureter. *J. Urol.*, 13: 15, 1931.
- BUMPUS, H. C., JR.: Urinary reflux. *Trans. Am. Assoc. Genito-Urin. Surg.*, 17: 17, 1924.
- BUMPUS, H. C., JR.: Ureteral meatotomy for removal of stones from the ureter. *J. Urol.*, 16: 359, 1926.
- CAMPBELL, M. F.: Diverticulum of the ureter. *Am. J. Surg.*, 34: 385, 1936.
- CAMPBELL, M. F.: Valvular obstruction of the ureters in children. *J. Urol.*, 36: 366, 1936.
- CAMPBELL, M. F.: Ureteral obstruction in children. *J. Urol.*, 41: 660, May 1939.
- CANTOR, M. O., *et al.*: Cystitis and pyelitis cystica, associated with multiple cysts of the kidney. *Urol. & Cutan. Rev.*, 37: 842, 1933.
- CARP, I. J.: Ureteral calculus, an analysis of 100 cases. *Urol. & Cutan. Rev.*, 41: 587, 1937.
- CARSON, W. J.: Pyelitis, ureteritis and cystitis cystica. *Am. J. Surg.*, 8: 1256, 1930.
- CECIL, A. B.: Aberrant renal vessels, a cause of kidney disease. *Surg. Clin. North Am.* 10: 983, 1930.
- CHEVASSU, M.: Kystes épithéliaux disséminés sur la muqueuse de l'urétéres. *Bull. Soc. franc. d'ur.*, p. 138, March 16, 1936.
- CHEVASSU, M.: L'urétére "gynécologique" à la lumière de l'urétéro-pyelographie rétrograde. *Mem. Acad. de chir.*, 62: 1194, 1936.
- CHEVASSU, M.: Kystes épithéliaux disséminés sur la muqueuse du bassin et de l'urétére des deux côtés. *Diagnostic par l'urétéro-pyelographie rétrograde. J. d'ur.*, 41: 483, 1936.
- CHURCH, C. K.: Stricture of ureter. its etiology and treatment. *N. Y. State J. M.*, 27: 1, 1927.
- CLELAND, J. B.: Ureteritis cystica. *M. J. Australia*, 13: (2): 13, 1926.
- COCHENS, F. M., AND GRAUER, T. F.: Squamous-cell carcinoma, leukoplakia, and concretions of a megaloureter. *J. Urol.*, 34: 106, 1935.
- COLEMAN, S. R.: Management of unilateral calculus obstruction of the ureter. *Med. Bull. Vet. Admin.*, 14: 260, 1938.
- COLSTON, J. A. C.: Primary tumor of the ureter. *Johns Hopkins Hosp. Bull.*, 56: 361, 1934.
- COLSTON, J. A. C.: Symptomatology, diagnosis and treatment of ureteral calculi. *Surg. Clin. North Am.* 16: 1205, 1936.
- CONSTANTINESCO, P.: Le reflux vesico-ureteral, etc. *J. d'ur.*, 41: 247, 1936.
- CRANCE, A. M., AND KNICKERBOCKER, H. J.: Primary carcinoma (epithelioma) of the ureter: case. *J. A. M. A.*, 82: 1930, 1924.
- CREEVY, C. D.: Operative treatment of hydronephrosis due to obstruction at the uretero-pelvic junction. *Surgery*, 1: 228, 1937.
- CROSBIE, A. H.: Kinks of the ureter due to aberrant vessels. *Boston Med. & Surg. J.*, 188: 678, 1923.
- CULVER, HARRY: Papilloma of the ureter. *J. Urol.*, 6: 331, 1921.

- CULVER, HARRY: Congenital stricture at the ureteropelvic junction. *Surg. Clin. North America*, 14: 805, 1934.
- CULVER, H., AND BAKER, W. J.: *Unilateral hydro-ureteronephrosis without evidence of obstruction*. *Med. Clin. North America*, 17: 1553, 1934.
- DAVIS, R. L.: Diverticulum of the ureter. *J. Urol.*, 31: 473, 1934.
- DAWLEY, W. A.: Ureterocele. *Arch. Surg.*, 21: 458, 1930.
- DAY, R. V.: Uremia following ligation of both ureters in the course of hysterectomy. *J. A. M. A.*, 99: 1942, 1932.
- DAY, R. V.: The role of the ureter in renal tuberculosis. *Am. J. Surg.*, 22: 542, 1933.
- EISENDRATH, D. N.: Congenital strictures and spiral twists of the ureters. *Ann. Surg.*, 65: 552, 1917.
- EISENDRATH, D. N.: Ureteral strictures, kinks and abnormal inserts. *Surg. Gynec. & Obst.*, 41: 557, 1925.
- EISENDRATH, D. N.: Hydronephrosis due to obstruction of the renal pelvis by one or two main renal arteries. *J. Urol.*, 24: 173, 1930.
- EMMETT, J. L.: Technical points to promote safety in the manipulation of ureteral stone. *Proc. Staff. Mtg. Mayo Clinic*, 12: 449, 1937.
- ENGEL, W. J.: Injuries to the ureter in pelvic surgery. *Ohio State Med. J.*, 33: 862, 1937.
- ESCAT: Kyste hydatique du rein: évolution dans le bassin. *Assoc. franç. d'uro.*, Proc.-Verb 14^e Ses., p 468, 1910.
- FAURE, J. L.: Sur la protection de l'urétére dans l'extirpation des tumeurs du ligament large. *Medicine*, 16: 313, 1935.
- FEINER, D.: Operative injuries to the ureter. *Surg. Gynec. Obst.*, 60: 790, 1938.
- FITZGERALD, W.: Hydronephrosis resulting from accessory renal vessels. *Brit. J. Urol.*, 5: 151, 1933.
- FLEMING, J. P.: Ureteritis cystica: case report. *Glasgow M. J.*, 130: 81, 1938.
- FOLEY, F. E. B.: Management of ureteral stone; operation versus expectancy and manipulation. *J. A. M. A.*, 104: 1314, 1935.
- FOORD, A. G., AND FERRIER, P. A.: Primary carcinoma of the ureter. *J. A. M. A.*, 112: 596, February 18, 1939.
- FOULDS, G. S.: Urinary tract infections. *Bull. Acad. Med. Toronto*, 11: 278, 1938.
- FRANCOIS, JULES: Diagnostic et traitement des calculs de l'urétére. *J. d'uro.*, 39: 219, 1935.
- FRIEDMANN, L.: Einseitige uretergonorrhöe bei kongenitaler ostiumstenose. *Schweiz. med. Wchnschr.*, 67: 625, 1937.
- GEISINGER, J. F.: Extravasation from the ureter. *Ann. Surg.*, 93: 544, 1931.
- GILBERT, J. R.: Primary cancer of the ureter associated with ureteritis cystica: case report. *Urol. & Cutan. Rev.*, 40: 191, 1936.
- GILBERT, J. R.: Primary carcinoma of the ureter: case report and review of literature. *Surg. Clin. N. Am.*, 13: 448, 1933. *Also* *Am. J. Surg.*, 36: 711, 1937.
- GIORDANO, A.: Sull' idronefrosi e sull'idrouretere congeniti. *Arch. ital. di urol.*, 11: 158, 1934.
- GRANTHAM, W. L.: Diverticulum of the ureter. *Southern M. J.*, 23: 792, 1930.
- GRUBER, C. M.: The function of the uretero-vesical valve and the experimental production of hydro-ureters without obstruction. *J. Urol.*, 23: 161, 1930.
- GUTIERREZ, R.: The modern surgical treatment of ureterocele. *Surg. Gynec. & Obst.*, 68: 611, March 1939.
- HAGER, B. H.: Prostigmin in the treatment of ureteral calculi, etc. *Trans. Am. Assoc., Genito-Urin. Surg.*, 30: 291, 1937.
- HAMER, H. G., et al.: Ureteral granuloma. *J. Urol.*, 29: 43, 1933.
- HARLOW, T. W., AND AFIFI, M. A.: Some observations on the diagnosis and treatment of bilharziasis of the urinary tract. *Urol. & Cutan. Rev.*, 34: 575, 1930.

- HARRIS, A.: Operative injury to the ureter: 5 cases. *Am. J. Surg.*, 8: 801, 1930.
- HARRIS, H.: The problem of non-calculous ureteropelvic obstruction. *Ann. Surg.*, 102: 1050, 1935.
- HARVIER, P., *et al.*: Répercussions vasculaires de divers traumatismes urétéro-pyéliques. *Paris méd.*, 1: 398, 1938.
- HENLINE, R. B.: Traumatic injuries of the upper urinary tract following instrumentation. *J. A. M. A.*, 102: 182, 1934.
- HERMAN, LEON: Quoted by Bloch and Jomain.
- HIGGINS, C. C.: Primary carcinoma of the ureter. *Ann. Surg.*, 108: 271, 1938.
- HILLIARD, C.: Congenital dilatation of the ureter. *Brit. M. J.*, 2: 838, 1935.
- HINMAN, F.: *The Principles and Practice of Urology*. P. 474. Phila., W. B. Saunders Co., 1935.
- HINMAN, F., *et al.*: Pyelitis and ureteritis cystica. *J. Urol.*, 35: 174, 1936.
- HOLMES, R. J., AND COPLAN, M. M.: The management of ureteral calculi. *Southern M. J.*, 29: 673, 1936.
- HOSFORD, J. P.: Some factors in the causation of hydronephrosis. *Lancet*, 1: 435, 1932.
- HUNNER, G. L.: Ureteral stricture: report of 100 cases. *Johns Hopkins Hosp. Bull.*, 29: 323, 1918.
- HUNNER, G. L.: The etiology of ureteral calculus. *Surg. Gynec. & Obst.*, 27: 252, 1918.
- HUNNER, G. L.: Intractable bladder symptoms due to ureteritis. *J. Urol.*, 4: 503, 1920.
- HUNNER, G. L.: Ureteral stricture an important etiologic factor in the so-called essential hematuria. *J. A. M. A.*, 79: 1731, 1922.
- HUNNER, G. L.: Calculus of the urinary tract, treated by new methods. End results. *Trans. Southern Surg. Assoc.*, 40: 1, 1927.
- HUNNER, G. L.: Ureterocoele: report of 10 cases. *Urol. & Cutan. Rev.*, 39: 755, 1935.
- HUNNER, G. L.: Ureteral stricture; its frequency and diagnosis. *Southern M. J.*, 34: 885, 1941.
- HUNNER, G. L.: Bright's disease: ureteral stricture an important etiologic factor. *Southern M. J.*, 35: 577, 1942.
- HUNNER, G. L.: Ureteral stricture and Bright's disease; report on 9 illustrative cases. *J. Urol.*, 49: 77, 1943.
- HUNTER, A. E.: Primary tumor of the ureter; end results in 3 cases. *J. Urol.*, 33: 443, 1935.
- IBRAHIM, A. B.: Bilharziasis of the ureter. *Lancet*, 2: 1184, 1923.
- INGHAM, R. O., AND MARTIN, W. F.: Unusual symptoms due to kink and stricture of the ureter, etc. *Urol. & Cutan. Rev.*, 42: 7, 1938.
- JACOBY, M.: Hypernephroide krebs der niere kombiniert mit nierenbeckenstein, papillarer krebs des nierenbeckens und harnleiters, ureteritis cystica. *Ztschr., f. Urol.*, 23: 718, 1929.
- JENKINS, JAMES A.: Ureteric injury. *Brit. J. Urol.*, 10: 252, September 1938.
- JOELSEN, J. J.: Pyelitis, ureteritis, and cystitis cystica. Report of case showing urographic evidence of lesion in ureters and pelves. *Arch. Surg.*, 18: 1570, 1929.
- KALO, A.: Die behandlung bei kleinbeckenoperationen vorkommenden harnleiterverletzungen. *Bruns' Beitr. z. klin. Chir.*, 168: 33, 1938.
- KIMBALL, F. N., AND FERRIS, H. W.: Papillomatous tumor of renal pelvis associated with similar tumors of the ureter and bladder: review of literature and report of 2 cases. *J. Urol.*, 31: 257, 1934.
- KINDALL, LLOYD: Pyelitis cystica and ureteritis cystica. *J. Urol.*, 29: 645, 1933.
- KIRWIN, T. J.: Diseases of the ureter. *Cyclopedia of Medicine* (Piersol), p. 646. Phila., F. A. Davis Co.
- KIRWIN, T. J.: The role of the ureter in diseases of the genito-urinary tract. *Am. J. Surg.*, 4: 355, 1928.

- KIRWIN, T. J.: The clinical value of experimental ureteral implantation. *Am. J. Surg.*, 23: 14, 1934.
- KRETSCHMER, H. L.: Leukoplakia of the bladder and ureter. *Surg. Gynec. & Obst.*, 31: 325, 1920.
- KRETSCHMER, H. L.: Primary carcinoma of the ureter. *Surg. Gynec. & Obst.*, 38: 47, 1924.
- KRETSCHMER, H. L.: Leukoplakia of the urinary organs. *Surg. Gynec. & Obst.*, 47: 145, 1928.
- KRETSCHMER, H. L.: Duplication of the ureters—so-called diverticulum of the ureter. *J. Urol.*, 31: 61, 1933.
- LANDWÜST, C. VON: Vesical ureterocele. *Ztschr. f. urol. Chir.*, 20: 439-53, 1926.
- LAURENT ET DELVIGNE: Tumeur papillomateuse du bassin et de l'urètre, diagnostiquée par pelvographie rétrograde par injection de thorostat. *Liege méd.*, 27: 129, 1934.
- LAZARUS, J. A.: Primary tumors of the ureter, with special reference to the malignant tumors. *Ann. Surg.*, 99: 769, 1934.
- LAZARUS, J. A.: Cystic dilatation of the lower end of the ureter: special reference to the transurethral treatment with the high frequency cutting current: 2 cases. *J. Urol.*, 36: 139, 1936.
- LECOMTE, R. M.: Gunshot wound of the ureter. *J. Urol.*, 26: 447, 1931.
- LEGUEZ AND PAFIN: Dilatation double des urétéres d'origine tuberculeuse. *Bull. Soc. franç. d'urolog.*, 1: 86, 1922.
- LJUNGBERG, E., AND WAHLGREN, T.: Ein fall von nierenbecken-und harnleiter tuberkulose, etc. *Acta Radiol.*, 18: 213, 1937.
- LIVERMORE, G. R.: Ureteral calculi. *Am. J. Surg.*, 20: 214, 1933.
- LOWENTHAL, H. F., AND ROBERTS, R. A.: Bilharzia affecting the left ureter primarily. *Lancet*, 2: 706, September 29, 1934.
- LOWSLEY, O. S., AND TWINEM, F. P.: Differential diagnosis of pain in right side of abdomen, with special reference to urologic lesions. *Trans. Sect. Urol., J. A. M. A.*, p. 105, 1929.
- MACKENZIE, D. W., AND COCHRANE, W. J.: A preliminary report on the bacteriology of ureteral cultures. *J. Urol.*, 12: 113, 1924.
- MACMYN, D. J.: On dilatation of the ureters and hydronephrosis in childhood. *Brit. J. Urol.*, 1: 150, 1929.
- MAHN, B., AND ISRAEL, S. L.: Vaginal ureterolithotomy; review of literature and report of 2 cases. *Med. J. & Rec.*, 135: 529, 1932.
- MATHÉ, C. P.: The role of aberrant vessels in the production of hydronephrosis. *J. Urol.*, 19: 211, 1928.
- MATHÉ, C. P.: The diagnosis and present-day treatment of ureteral stone. *J. Urol.*, 28: 133, 1932.
- MATHÉ, C. P., AND DE LA PENA, L.: Primary carcinoma of the ureter. *Calif. & West. Med.*, 42: 357, 1935.
- MAYO, W. J., BRAASCH, W. F., AND MACCARTY, W. C.: Relation of anomalous renal blood vessels to hydronephrosis. *J. A. M. A.*, 52: 1382, 1909.
- McKAY, R. W.: Congenital hypertrophic ureteropelvic obstruction. *Am. J. Surg.*, 11: 67, 1931.
- MELICOW, M. M., AND FINDLAY, H. V.: Primary benign tumors of the ureter: review of literature and report of a case. *Surg., Gynec. & Obst.*, 54: 680, 1932.
- MERCIER, O.: Le prolapsus intravesical de l'extrémité inférieure de l'urètre. *J. d'urolog. méd. et chir.*, 19: 402, 1925.
- MOORE, T. D.: Factors determining management of ureteral calculi: improved method of cystoscopic removal. *J. Urol.*, 37: 1, 1937.

- MORGAN, J. L.: Diverticulum of the ureter. *Urol. & Cutan. Rev.*, 39: 377, 1935.
- MORRIS, H. L., AND BRUNTON, J. F.: Accidents sustained by the genito-urinary system during operative procedures. *Urol. & Cutan. Rev.*, 37: 145, 1933.
- MORSE, H. D.: The etiology and pathology of pyelitis cystica, ureteritis cystica, and cystitis cystica. *Am. J. Path.*, 4: 33, 1928.
- MOUKHARINSKY, A.: De l'urétérocele. *J. d'uro.*, 38: 1, 1934.
- MUNGER, A. D.: Management of calculi in the lower third of the ureter. *Am. J. Surg.*, 39: 584, March 1938.
- NESBIT, R. M.: Advanced bladder and urethral tuberculosis, etc. *Am. J. Surg.*, 22: 547, 1933.
- NEWELL, Q. U.: Injury to ureters including accidental ligation during pelvic operations. *Am. J. Obst. & Gynec.*, 25: 220, 1933.
- O'CONOR, V. J., AND JOHNSON, A. B.: Ureterocele: a clinical study of 19 cases. *J. Urol.*, 23: 33, 1930.
- OPPENHEIMER, G. D.: Nephrectomy vs. conservative operation in unilateral calculus disease of the upper urinary tract. *Surg. Gynec. & Obst.*, 65: 829, 1937.
- PACK, G. T., AND LE FEVRE, R. G.: The age and sex distribution and incidence of neoplastic diseases at the Memorial Hospital, New York City. *J. Cancer Res.*, 14: 167, 1930.
- PAPIN, M.: Epithélioma de l'urètre. *Bull. Soc. franc. d'uro.*, 17: 325, 1924.
- PARK, W. H., AND WILLIAMS, A. W.: Pathogenic microorganisms. Ed. 10. Phila., Lea & Febiger, 1933.
- PATCH, F. S.: Association between leukoplakia and squamous-cell carcinoma in the upper urinary tract. *New England J. M.*, 200: 423, 1929.
- PATCH, F. S.: Granuloma of the ureter. *J. Urol.*, 25: 193, 1931.
- PATCH, F. S.: Pyelitis, ureteritis, and cystitis cystica. *Trans. New England Branch Am. Urol. Assoc.*, p. 27, 1938.
- PATCH, F. S.: Transplantation of the ureter in hydronephrosis due to pressure of aberrant blood vessels. *Urol. & Cut. Rev.*, 39: 636, 1935.
- PATCH, F. S.: The genesis and development of Brunn's nests and their relation to cystitis cystica, cystitis glandularis, and primary adenocarcinoma of the bladder. *Canad. Med. Assoc. J.*, 33: 597, 1935.
- PATCH, F. S.: Primary tumors of the ureter. *Urol. & Cutan. Rev.*, 42: 625, September 1938.
- PETILLO, DROMEDE: Ureterocele: clinical significance and process of formation. *Surg. Gynec. & Obst.*, 40: 811, 1925.
- PLAYER, L. P.: Primary ureteral carcinoma, with case report and review of the literature. *Urol. & Cutan. Rev.*, 32: 433, 1928.
- PUGH, W. S.: Ureteral kinks. *Internat. J. Med. & Surg.*, 47: 355, 1934.
- QUINBY, W. C.: Factors influencing the operative procedure in hydronephrosis. *J. Urol.*, 38: 673, 1937.
- RANDALL, ALEXANDER: An hypothesis for the origin of renal calculus. *New England M. J.*, 214: 234, 1936.
- RANDALL, ALEXANDER: Obstructive uropathy. *Rhode Island M. J.*, 22: 175, 1939.
- RASCHE, C., AND BACON, S. K.: Primary neoplasms of the ureter: report of 2 cases and review of literature. *J. Urol.*, 39: 44, January 1938.
- RAVICH, A.: A critical study of ureteral calculi. *J. Urol.*, 29: 171, 1933.
- RHODES, J. S.: The clinical importance of ureterocele. *J. Urol.*, 35: 300, 1936.
- RILEY, AUGUSTUS: Nephropexy for ureteral kinks. *Am. J. Surg.*, 27: 534, 1935.
- ROONE, N. W.: Cystic disease of the urinary tract epithelium. *Canad. M. A. J.*, 40: 13, January 1939.
- ROVING, T.: Erfahrungen über uretersteine. *Monschr. f. urol.*, 6: 385, 1901.

- ROUSSELOT, L. M., AND LAMON, J. A.: Primary carcinoma of the ureter: report of case and review of literature. *Surg. Gynec. & Obst.*, 1: 17, 1930.
- RUDNICK, D. F., AND CORNELL, E. L.: Clinical manifestations of stricture of the ureter in women. *J. Urol.*, 41: 679, May 1939.
- SAINT, J. H.: Intravenous pyelography in a series of cases after transplantation of the ureters. *Brit. J. Surg.*, 23: 580, 1936.
- SCHILLINGS, M., AND SONDERVORST, F. A.: Les tumeurs malignes primitives de l'urètre. *Rev. belge Sc. Med.*, 8: 16, 1936.
- SCHREIBER, M.: Ureteral stricture; its anatomical and pathological background; based upon the findings in 100 consecutive autopsies. *Surg. Gynec. & Obst.*, 45: 423, 1927.
- SCOTT, W. W.: Primary carcinoma of the ureter. *Surg. Gynec. & Obst.*, 58: 215, 1934.
- SISK, IRA R.: Operative injuries of the ureter. *Surg. Gynec. Obst.*, 60: 857, 1935.
- SISK, I. R., AND WEAR, J. B.: Gonococcal infections of the kidney, ureter, and bladder. *J. Urol.*, 28: 639, 1930.
- SNYDER, W. H., AND WOOD, B. S.: Primary carcinoma of the ureter, with report of a case. *J. Urol.*, 29: 577, 1933.
- SOLIS-COHEN, L., AND BRUCK, S.: Horseshoe kidney, congenital bilateral hydronephrosis and hydro-ureter. *Pa. Med. J.*, 37: 819, 1934.
- SPIESS, P.: Die primäre epitheliale Tumoren des Nierenbeckens und des Ureters. *Centralbl. f. allg. Path. u. path. Anat.*, 26: 553, 1915.
- STANTON, E. M.: Actinomycosis limited to the urinary tract. *Am. Med.*, 11: 401, 1906.
- STEVENS, A. R.: Schistosomiasis involvement of the upper urinary tract. *Trans. Am. Assoc. Genito-Urin. Surg.*, 28: 275, 1935.
- STEVENS, W. E.: Accidental operative injuries of the female ureter. *J. Urol.*, 31: 74f, 1934.
- STEWART, R. L.: Primary tumors of the ureter. *Brit. J. Surg.*, 13: 667, 1925-26.
- STOW, B.: Ureteritis cystica chronica. *Ann. Surg.*, 46: 233, 1907. Also: *Proc. N. Y. Path. Soc.*, 7: 1, 1907.
- THOMAS, G. J., AND BARTON, J. C.: The role of congenital anomalies in the production of urological conditions in children, with special mention of congenital idiopathic dilatation of the ureter. *J. Urol.*, 33: 611, 1935.
- THOMSON-WALKER, SIR J.: Ureterectomy for papilloma; 3 cases with comments. *Brit. J. Urol.*, 1: 141, 1929.
- THOMSON-WALKER, SIR J., AND BARRINGTON, F. J. F.: Case of malakoplakia. *Proc. Roy. Soc. Med.*, 16: Sect. Urol., p. 32, 1922-23.
- TUASON, M. N.: Ureteritis and strictures of the ureter: 6 cases. *J. Philippine Is. Med. Assoc.*, 3: 300, 1923.
- VALVERDE, B.: Un cas de gomme ulcérée primitive de l'urètre: manifestation d'hérédosyphilis tardive. *Ann. d. mal. ven.*, 18: 614, 1923.
- VERMOOTEN, V.: Elongation of the ureter. *J. Urol.*, 23: 427, 1930.
- VERMOOTEN, V.: Bilharziasis of the ureter, and its pathognomonic roentgenographic appearance. *J. Urol.*, 38: 430, 1937.
- VERMOOTEN, V.: Bacillus coli infections of the urinary tract. *South African Med. J.*, 11: 767, 1937.
- VERMOOTEN, V., AND NEUSWANGER, C. H.: Effect on the upper urinary tract in dogs of incompetent ureterovesical valve. *J. Urol.*, 32: 330, 1934.
- VINCENT, G.: Les lésions de l'urètre produites au cours des interventions gynécologiques. *J. d'obst. et de gynec.*, 2: 9, 1931.
- VON LIMBECK, R.: Zur kenntnisse der epithel cysten der harnblase und der ureteren. *Ztschr. f. Heilk.*, 8: 55, 1887.
- VOSE, S. N.: Gunshot wound of the ureter. *New England J. Med.*, 206: 1075, 1932.

- VOSE, S. N.: Hydronephrosis due to subepithelial fibrosis; treatment by an adaptation of Rammstedt's technique. *New England. J. Med.*, 102: 786, 1934.
- WALTERS, G. A. B.: Primary benign neoplasms of the ureter. *Brit. J. Surg.*, 20: 682, 1933.
- WATERS, C. A.: Obstruction of the ureteropelvic junction due to aberrant blood vessels. *Am. J. Roent.*, 37: 756, 1937.
- WESSON, M. B.: Rupture of the ureter; a medico-legal problem; cases. *Calif. & West. Med.*, 37: 296, 1932.
- WIESING, P. J., AND BLIX, C.: Primary cancer of the right ureter. *Hygeia*, 40: 468, 1878.
- WILLIAMS, E. R.: Ureterocele. *Brit. J. Radiol.*, 9: 59, 1936.
- WINSBURY-WHITE, H. P.: Leukoplakia in the urinary tract: case. *Brit. J. Surg.*, 20: 49, 1932.
- WOODRUFF, S. R.: The management of ureteral calculus. *J. Med. Soc. New Jersey*, 35: 197, 1938.
- YOUNG, H. H.: Obstruction to the ureter produced by aberrant blood vessels. *Surg. Gynec. & Obst.*, 44: 26, 1932.



CHAPTER XXXV

OPERATIVE TREATMENT OF THE URETER

Preoperative Preparation

The evening before the operation the patient is given a soapsuds enema and a sedative. For the latter, phenobarbitol or nembutol, 0.1 Gm., is satisfactory. If regional anesthesia is to be used, the patient is permitted a light breakfast and fluids.

One hour before operation he is given additional analgesic by mouth (phenobarbitol or nembutol, 0.2 Gm.).

Preparation of Operative Field

The skin of the suprapubic region, abdomen, and back is cleansed with tincture of green soap and warm water, followed by alcohol, and sprayed with tincture of mercuriolate, 1:1,000 or tincture of zephiran, 1:1,000.

Anesthesia

In our clinic, ureteral operations in adults are practically always done under spinal anesthesia. For children and highly nervous adult patients, a general anesthetic is usually necessary.

Surgical Treatment of Ureteral Anomalies

DUPLICATION OF THE URETER

The surgical treatment of double ureter is that required for the associated pathology. Hydronephrosis, infection, and stone are the most common complications. If the renal parenchyma is extensively infected, nephro-ureterectomy will be necessary. In cases of double kidneys, which present calculi, hydronephrosis, or infection of the supernumerary kidney, heminephrectomy is the operation of choice, providing the other segment on the same side is free of infection. If, however, either of the double kidneys is the site of a tuberculous infection, complete nephro-ureterectomy is advisable, if the kidney on the opposite side is competent. Since heminephrectomy in such cases may leave a permanent fistula.

A blind-ending accessory ureter bifurcating from a normal ureter usually requires resection in order to save the kidney from the effects of

back pressure and infection. The accessory duct is resected at its place of origin, in such a manner that there is some of the redundant tissue left in place, in order to prevent stricture-formation. If obstruction and infection have been prolonged, nephro-ureterectomy may be necessary. In a case reported by Vormann (1929) the patient had had pain for 12 years and had undergone 4 major operations—nephropexy, cholecystectomy, appendectomy, and severance of "abdominal adhesions." Resection of the accessory blind-ending ureter was followed by complete relief of pain.

URETERS WITH EXTRAVESICAL OPENINGS

Many forms of surgical treatment have been utilized for ureters opening extravasically: ligation of the ureter, implanting the ureter into the bladder or intestines, anastomosing the pelves of double kidneys, or anastomosing ureter to ureter, or ureter to pelvis, nephrectomy or nephro-ureterectomy, heminephrectomy or heminephro-ureterectomy.

The choice of surgical procedure depends on the conditions in the individual case, namely, whether the ectopic ureter is single or from a duplicated kidney; the location of the ectopic ureteral orifice; the amount of renal tissue drained by the accessory ectopic ureter; the presence or absence of infection or other pathological changes in any segment of either ureter or kidney; the function of the portions of the kidney and of the opposite kidney; and the distribution of the vascular supply to the two segments.

In cases where the segment of kidney drained by the ectopic ureter is doing only a small part of the total work of that side, and there is no infection, simply ligating the ureter through the vagina or by the abdominal route may suffice.

An ectopic ureter may be reimplanted into the bladder (ureteroneocystotomy), either through the vagina or by the abdominal route—preferably the latter. Occasionally, a communication can be established between the ureter and the bladder with the cautery or electric cutting instrument through the cystoscope. Reimplantation of the ureter into the bladder is indicated when the ectopic ureter is that of a solitary kidney or the single ureter of a kidney that is worth saving. It is also indicated when the ectopic ureter drains half of a double kidney on one or both sides of the body, providing the segment of kidney is free of disease and has good function, and that the ureter itself is not distended or infected.

Usually, in the case of unilateral or bilateral ectopically ending ureters

which arise from one half of a double kidney, the operation of choice is heminephrectomy, which can generally be done fairly easily, since the upper and lower poles nearly always have independent blood supplies. There is some difference of opinion as to whether or not a ureterectomy should be done with the heminephrectomy, although most operators feel that it should.

In a majority of the reported cases of unilateral double ureter ending ectopically and corresponding to the two halves of a double kidney, complete nephrectomy was done. It may be possible, however, to re-implant one or both ureters into the bladder, if the opposite kidney is not adequate to carry on life, or if the double kidney on the involved side is wholly or partly worth saving.

Nephro-ureterectomy is indicated in marked disease of the entire kidney, or in occasional cases where technical difficulties may make heminephrectomy impossible, or when other procedures fail—if there is a satisfactorily functioning kidney on the opposite side.

Anastomosis—of pelvis to pelvis, ureter to pelvis, or ureter to ureter—is frequently a satisfactory method when other operations are not possible.

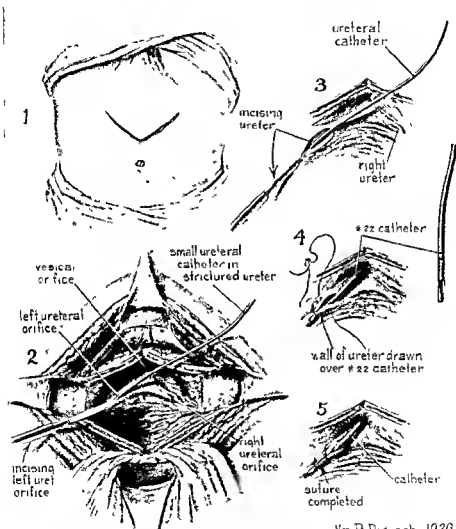
Surgical Treatment of Stenosis of the Uterovesical Orifice

A congenitally stenosed uterovesical orifice, or one constricted by scar tissue, which does not respond to attempts at dilatation, may frequently be enlarged through the cystoscope by means of cystoscopic scissors or the fulguration tip. If cold instruments are used, bleeding will have to be controlled by application of the cautery point.

The orifice may also be enlarged through a cystotomy opening. The usual method is to cut the orifice through the vesical wall and into the adjoining wall of the ureter. The mucous membrane of the ureter is then sutured to that of the bladder.

Another procedure is that of von Lichtenberg. The bladder is opened by suprapubic incision. A Reverdin needle is introduced into the ureteral orifice and carried up the ureter for a distance of from 2 to 3 cm. (making certain to pass beyond the strictured area), and the needle brought through the wall of both the ureter and bladder. A heavier suture is then passed by the same route but in the opposite direction. The two sutures are tied tightly enough to cause devitalization of the included tissue, with subsequent sloughing. In female patients, the suture ends are brought through the urethra; in males they must be

brought out through a small suprapubic drain. In 7 or 8 days the suture will slough out, leaving a normal-appearing slit, which functions well as a ureteral orifice and shows no tendency to reform the stricture.



Am P Dicusch 1929

Surgical Treatment of Non-Calculous Obstructions at the Ureteropelvic Junction

There is wide divergence of opinion concerning the treatment of obstructions at the ureteropelvic junction, due to the fact that the end-

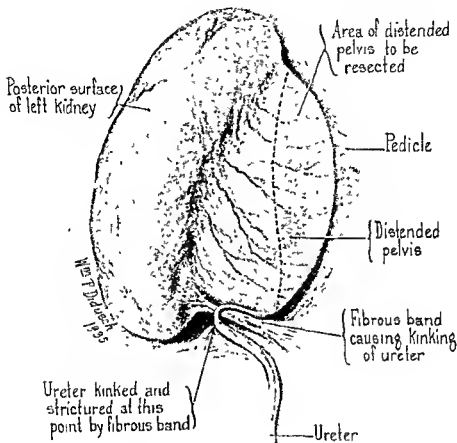
results in plastic surgery of this region in the past have not been entirely satisfactory, particularly in children. In many of these cases, the destruction of the kidney, from back pressure and infection, is such that only nephrectomy will avail. However, the purpose of renal and ureteral surgery (except in malignant disease and tuberculosis) should be to conserve all functioning kidney tissue, if this can be done with safety to the patient. Hydronephrosis, in particular, often lends itself to conservative surgery. Even when there is fairly marked dilatation of the pelvis and calyces and thinning of the cortex, the kidney may be well worth saving, and conservatism by plastic operation, rather than nephrectomy, is indicated in many cases. Hydronephrosis due to stenosis or other obstruction at the ureteropelvic junction frequently manifests itself early in life, and the conserved organ may prove a life-saving factor should disaster later befall the opposite kidney.

Conservative surgery by plastic operation, rather than nephrectomy, is indicated (1) when the obstruction can be relieved by a plastic procedure, (2) when there is enough functioning tissue to make the kidney worth saving, (3) in the absence of the opposite kidney or severe impairment of its function.

Types of Operations. Many types of plastic operations have been suggested for hydronephrosis due to obstruction at the ureteropelvic junction, indicating the uncertainty with which this problem is approached.

The first deliberate conservative operation for obstruction at the ureteropelvic junction was probably that of Kuester (1891), who, in the presence of a hydronephrosis due to stenosis at the junction, resected the ureter below the stenosis and reimplanted it into the most dependent portion of the pelvis. This method has been used since, with but slight modifications, by von Lichtenberg, Wildbolz, W. C. Quimby, Walters, and others. Some of these technics employ end-to-end anastomosis and others side-to-side anastomosis, while the von Lichtenberg operation allows the cut end of the ureter to project into the pelvis for a short distance, the latter being sutured about it like a cuff. The objections to ureteropyeloneostomy are (1) the possibility of inducing a recurrence of the stricture at the point of anastomosis, and (2) the fact that it interrupts the continuity of the ureter with the pelvis, and may hinder or inhibit peristalsis. Despite these criticisms, better results have been reported from resection of the ureter (using an oblique incision) and reimplantation into the most dependent portion of the pelvis than from most other

methods. The work of Deming and his colleagues has shown that if the ureter intrudes about 2 cm. into the pelvis, stricture is less likely to result. We have employed both end-to-end anastomosis and the von Lichtenberg operation, with excellent results. Diversion of the urinary stream by

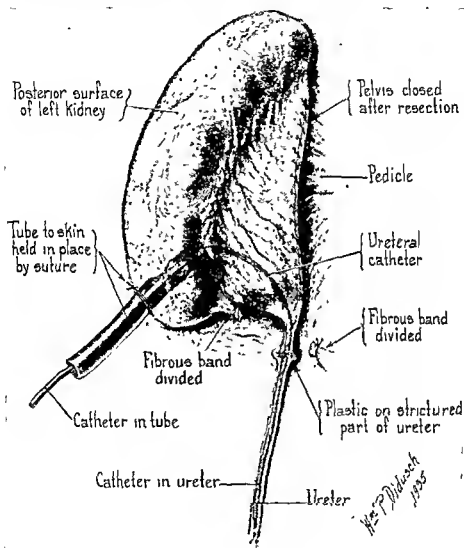


the area of distended pelvis to be resected. (Case of Dr. Roy B. Henline)

prolonged nephrostomy, combined with splinting of the ureter with a ureteral catheter inserted through the nephrostomy wound, are essential to the success of this procedure.

In 1894 Fenger applied the Heineke-Mikulicz operation for pyloric stenosis to stenosis at the ureteropelvic junction. Although sometimes

successful, it frequently is followed by mechanical buckling of the ureter opposite the site of operation—a fact which has caused some surgeons to discard this operation altogether. Figures 289 and 290 show a case successfully operated upon by this method.



ARCHIVE

Schwytzer (1923) used a Y-shaped incision on the ureter and pelvis to form a flap which was sutured down the ureter to enlarge the uretero-

pelvic outlet. He first divided the posterior surface of the upper inch of the ureter by a longitudinal incision, which was then prolonged upward upon the pelvis to form a V. The apex of the triangular flap of pelvic wall thus outlined was pulled down to the lower end of the incision in the ureter and closed as a V, thus widening the junction without interrupting the continuity of the ureter, or causing it to twist or kink.

Foley (1937) modified this procedure by making the longitudinal incision on the lateral aspect of the ureter, and placing one limb of the V on the anterior surface of the pelvis and the other on the posterior surface. When these incisions are sutured, the pelvis is placed in a dependent position which promotes drainage. In neither of these operations is there the formation of spurs between the ureter and pelvis.

Some success has followed the utilization of the Rammstedt pyloroplasty type of procedure, which was first applied to the ureter by D. M. Davis (1933), and consists in cutting through the strictured ureteral wall down to, but not penetrating, the mucosa, and permitting the incision to remain open. A large ureteral bougie or catheter should be left in the ureter for several days, to make certain that it remains open, and the procedure should be combined with nephrostomy, for adequate drainage.

Importance of Determining Exact Cause of Obstruction Before Instituting Surgery. The proper recognition and evaluation of the etiological factor or factors involved is the first requisite to successful surgical treatment of obstruction at the ureteropelvic junction. Most obstructions at this point, as we have previously seen, are due to one or more of the following conditions: (1) stenosis at the ureteropelvic junction, which may be (a) congenital or (b) acquired; (2) high insertion of the ureter; (3) hypertrophy of the ring muscle at the ureteropelvic junction; (4) kinking of the ureter; (5) aberrant renal blood vessels. Frequently more than one factor is responsible, and it may then be difficult to determine the primary cause and which factors are merely secondary. The presence of obstruction can be shown by pyelography, but the determination of the exact cause must usually be done at the operating table.

Although the opinion still prevails that aberrant renal vessels are the chief cause of non-calculous obstructions at the ureteropelvic junction, much careful investigation has shown such vessels to be the *primary* cause in but a relatively small percentage of cases. Geraghty and Frontz, Gibson, O'Connor, McIver, and Campbell have all found intrinsic stenosis to be the most frequent primary cause, and this has also been our experience. Undoubtedly many such constrictions within the ureter are

overlooked, particularly when an aberrant vessel or a fibrous band is discovered at operation. When stenosis and an aberrant vessel co-exist, both must be corrected to establish adequate drainage. Merely severing an aberrant vessel or fibrous band outside the ureter, while a constriction within the ureter—the actual cause of the obstruction—goes unrecognized and untreated, will not relieve the obstruction, which will persist until renal damage eventually requires nephrectomy.

Henline and Menning have recently published a very complete study of 14 cases (4 of them bilateral) of non-calculous obstruction at the ureteropelvic junction treated by operation at the Brady Foundation, of the New York Hospital, within the past 1½ years. In these 18 kidneys the following obstructive conditions were found at operation:

Stenosis .	15: stenosis alone. 9
	stenosis and aberrant vessels... . 3
	stenosis and kinking 2
	stenosis, aberrant vessel, and high insertion of the ureter... . 1
High insertion of the ureter	2: with aberrant vessel (no stenosis) 1
	with aberrant vessel and stenosis..... 1
Marked hypertrophy of the ring muscle . . .	1: (lesser degree in others)
Accessory renal vessels . . .	6: regarded as sole etiological factor in only 1 (and that erroneously, the symptoms returning 6 weeks after severance of the vessel and pyelograms showing persistence of obstruction)

Even at the operating-table the diagnosis of ureteropelvic stenosis may present considerable difficulty. Often the external circumference of the ureteropelvic junction appears entirely normal, and one must then determine not the outer circumference, but the *inner* caliber of the ureter. When palpation leaves doubt regarding the caliber of the ureteral lumen at this point, it is our practice at the Brady Foundation to follow the method suggested by Bidgood and Roberts, namely, after severing adhesions between the renal pelvis and the ureter, inject 10 to 20 cc. of saline into the renal pelvis with a fine needle (the amount depending on the size of the hydronephrosis), then observe the peristalsis of the pelvis and upper portion of the ureter. Delayed emptying, with the ureteropelvic junction freed from all extrinsic obstruction, indicates that some obstructive condition exists at this point which should be corrected. When this procedure also fails to convince us that there is no intrinsic

narrowing, we examine the ureteropelvic junction through an incision made in the lateral wall of the ureter at this point.

Reasons for Failure in Plastic Operations on the Ureteropelvic Junction. Failures have been frequent in plastic operations for ureteropelvic obstruction (nearly 30 per cent of cases, Mathé). Lubash and Madrid have summarized the main reasons for failure as follows: (1) leakage of urine from the anastomosis and resulting infection, (2) tension on the repair, (3) puckering at the site of repair, (4) new stricture-formation in an area bathed by urine, (5) persistent infection within the kidney, (6) urinary fistula.

Importance of Prolonged Nephrostomy Drainage and Splinting of the Ureter. If success is to be hoped for in plastic operations on the ureteropelvic junction, the above complications must be avoided. In this regard, Henline and Menning emphasize the extreme importance of prolonged nephrostomy drainage and splinting of the ureter. They state:

Prolonged nephrostomy drainage relieves tension on the repaired area by diverting the urine and places the newly sutured area at rest. With nephrostomy drainage, only minimal amounts of urine seep through the repaired area, and this for only a short time. An attempt should be made to so place the nephrostomy tube that urine will readily drain through it, thus avoiding extravasation around the repaired area. Such leakage, when prolonged or excessive, tends to cause excess scar-formation, which later may contract to produce a narrow ureteropelvic outlet.

Puckering at the site of repair may be avoided by selecting the proper type of repair. Renal infection usually can be controlled by prolonged nephrostomy drainage and the newer antiseptics.

Splinting the ureteropelvic junction with a soft rubber catheter (No. 10, 12, or 14-F.), placed through the nephrostomy wound and down the ureter, has been our customary practice during the past year. . . In all cases, the splinting catheter was allowed to remain in place for at least 6 weeks. . . . With adequate nephrostomy drainage, very little urine seeps through the repaired ureteropelvic junction, and peri-ureteral fibrosis is kept to a minimum. . . . Prolonged splinting permits the ureter to be well fixed in its new bed, with less likelihood of future contraction from the surrounding scar tissue. The lumen of the ureter is thus maintained to the size of the splinting catheter until the healing of the ureteropelvic junction is complete.

Selection of Type of Operation. *For stenosis at the ureteropelvic junction*, we prefer, in the majority of cases, to do a modification of the Y-plasty procedure first described by Schwyzer and later modified and popularized by Foley.

For high insertion of the ureter, we separate the ureter from the renal pelvis, remove the stenosed area when present, and reimplant the ureter into the most dependent portion of the pelvis. For this operation (ure-

teropyeloneostomy) we usually prefer an end-to-end anastomosis, but have also had success with von Lichtenberg's method mentioned above.

These two procedures—the Y-plasty operation and ureteropyeloneostomy—we have found to be the most satisfactory of the plastic operations devised for hydronephrosis due to ureteropelvic obstruction. Where there is a greatly redundant pelvis, prior to the performance of the Y-plasty, and occasionally of ureteropyeloneostomy, a portion of the redundant pelvis is excised. Aberrant vessels and fibrous bands are freed as indicated in each case.

In the 14 cases from our service, reported by Henline and Menning (mentioned above), the following operations were done upon the 18 obstructed kidneys:

Ureteropyeloneostomy	3: end-to-end anastomosis	2
(In 2 cases, for high insertion of the ureter; in 1, for impassable stenosis requiring resection of upper ureter)	von Lichtenberg operation	1
Nephrectomy		2
(For marked renal destruction)		
Severance of aberrant vessel		1
(No other surgery deemed necessary; postoperative return of symptoms)		
Foley Y-plasty operation	12: also severance of aberrant vessel	2
	also freeing of kinks	2
	also resection of fibromuscular ring	1

In every case where a plastic operation was performed on the ureteropelvic junction, a nephrostomy drain (Malecot catheter) and a splinting soft-rubber ureteral catheter were allowed to remain in position for 6 weeks.

Although this practice of prolonged nephrostomy drainage and splinting of the ureter in plastic repairs has been employed at the Brady Foundation less than 18 months, so that the end-results cannot as yet be properly evaluated, we have been greatly impressed with our immediate postoperative results. Postoperative pyelograms and 10-minute delayed films have shown that, in every instance, the kidney has drained more promptly, residual urine in the pelvis has been decreased or completely eliminated, the kidney function has improved, and the symptoms have been relieved. All of the 14 patients are free of infection except in 2 cases (*Bacillus proteus*), where stone-formation has occurred; both of these patients are symptom-free.

When an aberrant blood vessel is the sole cause of obstruction, or is causing

obstruction in conjunction with ptosis or undue mobility of the kidney, satisfactory results may be obtained by freeing the renal pelvis and upper part of the ureter, severing the offending vessel after ligation, and restoring the kidney and ureter to their normal positions by means of a nephropexy.

If the obstructing artery supplies a considerable area of kidney tissue, as proved by temporary compression, it will be necessary to do either (1) a ureteropyeloneostomy to circumvent the vessel, or (2) a plastic operation employing resection of part of the redundant renal pelvis, with closure in such a manner as to draw the offending vessel into a position where it will not obstruct the ureter.

H. H. Young (1932) put forward a method of resecting the renal pelvis in such a way that the ureter is drawn away from the aberrant vessel, thus doing away with the necessity of sectioning either the vessel or the ureter. Areas from the anterior and posterior walls of the dilated pelvis are excised. The pelvis is closed anteriorly in such a way as to draw the portion to which the aberrant vessel is attached upward and inward. The posterior wall is then sutured so as to draw the ureter upward and backward, using the Heineke-Mikulicz form of closure. A catheter is inserted in the ureter by being passed through a stab-wound in the pelvis. Additional drainage is furnished by a rubber tube sutured at the upper angle of the wound in closing.

Hellström resects the excess pelvis and sutures the offending vessels above the ureter's entrance to the pelvic wall; while Patch transversely severs the pelvis and re-sutures it on the other side of the anomalous vessels, above their level of entrance.

Technic of Modified Foley Y-Plasty Operation. The kidney is exposed through the usual lumbar incision, freed from the surrounding fascia, and delivered into the wound. Adhesions between the renal pelvis and ureter are severed, thus accurately exposing the ureteropelvic junction. The latter is carefully examined by inspection and palpation. If the outer circumference of the ureter at this point appears to be normal, but doubt exists regarding the *inner* caliber, 10 to 20 cc., or more, of saline is injected into the pelvis with a fine needle and the peristalsis of the freed ureteropelvic junction noted. If there is delayed emptying, with the adhesions severed, intrinsic stenosis is assumed to be present. If there is still doubt, the ureteropelvic junction is examined through an incision in the lateral wall of the ureter at this point.

The upper part of the ureter is then freed. A Malecot catheter (usu-

ally No. 20 to 26-F.) is pulled through the lower calyx by means of a curved clamp inserted from the pelvis through the cortex. Alongside the Malecot catheter is placed a soft rubber catheter (No. 10, 12, or 14-F.) passed through the nephrostomy wound and pelvis and down the ureter, to a point well below the site of repair, to be used as a ureteral splint.

A Y-incision is then made in accordance with the method of Foley, placing the longitudinal incision, or stem of the Y, on the lateral border of the ureter, one arm of the Y on the anterior surface of the pelvis, and the other on the posterior surface. The tip of the triangular-shaped flap of pelvic wall is sutured to the lower end of the ureteral incision by interrupted sutures of 0000 chromic catgut on an atraumatic needle, including all layers of the wall in the suture but attempting to get as accurate an approximation of tissue as possible. This leaves a Y-shaped draining ostium at the ureteropelvic junction, which promotes normal drainage.

The kidney is returned to its fossa; one Penrose drain is placed at the site of the nephrostomy drainage and another at the site of the repair. The wound is closed in layers—the drains, nephrostomy tube, and splinting catheter being brought out near its posterior angle.

Postoperative Care in Plastic Surgery on the Ureteropelvic Junction. Postoperatively, the Penrose drains are removed in 3 or 4 days. The nephrostomy tube and the splinting catheter are allowed to remain in position for 6 weeks to permit the repair and alignment of tissues to become complete.

During this period, the urine is carefully checked as to pH and evidences of infection. It is preferable to have the urine of these patients on the acid side, because an alkaline infection, such as that due to the *Bacillus proteus*, may lead to the deposition of calcium. We try to eradicate infection by (1) the proper handling of the drainage tubes, (2) attempts to make the patient's urine acid either by diet or by ammonium chloride and mandelic acid therapy, and (3) the use of chemotherapy, especially the sulfonamides, when necessary. Using the sulfa drugs in the wounds, as well as orally, has been most helpful in reducing infection in these cases.

Almost weekly flat plates are taken to rule out the deposition of calcium. Pyelograms are made at varying intervals, usually 3 and 6 weeks postoperatively, after injecting contrast solution through the nephrostomy tube. So long as there is evidence of extravasation of the contrast

solution outside the area of repair, the tube and splinting catheter are left in place. When healing is complete—usually within 6 weeks—both tubes are removed. As a rule, the renal sinus heals promptly—usually within 24 to 48 hours—indicating that the kidney is draining satisfactorily.

After the wound is healed, retrograde pyelographic studies are repeated, and the function and emptying time of the kidney carefully checked. These patients need very careful postoperative follow-up, and they should receive interval dilatations of the ureter, the intervals being gradually prolonged with the patient's symptoms and renal findings as a guide.

Operative Treatment of Ureteral Injury

INJURIES FOLLOWING URETERAL INSTRUMENTATION

Injuries of the ureter following instrumentation may be divided into two groups: (1) those in which the ureteral catheter or other instrument actually perforates the ureter (rare); (2) those where the ureter is cracked or split longitudinally, so that injected fluids rapidly seep out, as through a sieve (*Injuries of the Ureter*, p. 1232). The latter type of injury is fairly common, and may occur during any form of manipulation within the lumen when the tissues are irritated, edematous, or necrotic.

Extravasation of urine from such a break in the ureteral wall is, of course, a grave accident which calls for surgical drainage. Otherwise, surgery plays but a small part in the handling of these cases. Suture of the traumatized ureter may occasionally be necessary; this is generally done with fine silk or catgut. The sutures (interrupted or simple continuous) are carried through the outer and middle coats but not the mucosa.

The introduction of an indwelling catheter has proved, on the whole, the most useful and practical treatment. Experience has shown that interruption of the continuity of the ureteral wall—even fairly large slits and punctures—will heal, if given the support of a catheter which at the same time prevents leakage and diverts the urine from the edges of the wound during the healing process. In a series of 9 cases reported by Henline from the Brady Foundation for Urology, of the New York Hospital (1934), this simple expedient proved the best way of handling these ureteral injuries.

As in many other types of medical practice, the best treatment of instrumental ureteral injury is prevention. In exploring a ureter known to be,

or suspected of being, diseased, a stylet should not be used; or, if one must be used, it should never be extended to the tip of the catheter. All instrumentation should be conducted with the utmost deliberation and gentleness, and the dangers of rupture or perforation kept constantly in mind.

URETERAL INJURY INCURRED DURING SURGICAL OPERATION

The victims of this accident are generally women, as it most commonly happens during hysterectomy, particularly when done by the vaginal route. The ureter may be cut across so as to be completely severed; it may be perforated or cut at one point only; or, most frequent of all, it may be included in a ligature or suture so that the lumen is entirely occluded.

Every attempt to repair the ureter, and thereby save its kidney, should invariably be made if the slightest prospect of success can be held out. When repair is promptly attempted, the percentage of cases where at least partial restoration of function has been demonstrated is encouragingly large.

If the accidental inclusion of the ureter in a ligature is recognized immediately after operation, it may be possible to reopen the wound, cut the ligature, and restore the lumen of the ureter by the introduction, through the cystoscope, of a ureteral catheter, which may be passed through the point where the ligature was tied up to the pelvis. The catheter should be allowed to remain for at least 24 hours.

In an unusually interesting case reported by Brooks (1934) the patient suffered a double ligation during vaginal hysterectomy. In 24 hours the kidneys were enormously dilated. Nephrotomy, consisting of numerous "punctures" in the renal cortex, permitted the urine to drain out through a cutaneous opening, and after 4 or 5 days the sutures absorbed and urine began to flow from the ureteral orifices into the bladder. By the fifteenth day urination was normal.

If the ureter has been severed without loss of substance, anastomosis of the cut ends may be possible. Also, if the ureter has been too badly crushed or lacerated to give promise of healing, it may be possible to excise the lacerated portion and anastomose the remainder without exerting too much tension. If the injury is at or close to the vesical termination, the ureter may sometimes be freed from its normal implantation and reimplanted higher up on the bladder wall. The success of any method depends largely on the location of the injury, as tension

on the duct will vitiate the result and must always be avoided. If anastomosis or reimplantation cannot be performed without too great tension, and the opposite kidney has been proved capable of carrying on alone, the proximal end of the ureter is ligated and allowed to remain in the abdomen, and nephrectomy performed when the patient recovers from the shock of the primary operation. Needless to say, nephrectomy should be done only as a last resort, when repair by any method is impossible. When renal function on the opposite side is poor, nephrostomy, ureterostomy, or transplantation of the ureter to the intestine must be considered.

Anastomosis. Methods of joining a severed ureter are of two main types: (1) end-to-end anastomosis, and (2) invagination of the proximal segment into the distal segment. Fine silk or 00 chromic catgut is regularly used, the stitches passing through all the coats except the mucosal. Some methods require splitting of the distal end; others eliminate this, but require support of some kind until healing has taken place; while still others dispense with both splitting and support, as the invagination first suggested by Poggi and since modified by various operators.

In Poggi's original technic, the distal end of the ureter is dilated with a special type of forceps. One or two pairs of traction sutures are placed through the proximal end—two needles upon a single thread, introduced approximately 2 mm. distant from one another in the same horizontal plane. From within the lower end of the proximal portion of the ureter the needles are brought out, about 3 mm. apart, and passed from within outward in the distal end, the same distance apart and about 7 mm. to 1.3 cm. from the free end, so that they come out opposite the points where they were first introduced. The sutures are tied after traction has been exerted upon them sufficient to invaginate the proximal end into the distal end. Reinforcement of the invagination is accomplished by including all the coats of the distal fragment, and the fibrous and muscular coats of the proximal fragment, by continuous or interrupted sutures applied about the line of junction.

In Albarran's method, the divided ends of the ureter are brought into contact, and 3 non-penetrating Lembert sutures are set by pushing the needle from within outward, so as to "hinge together" the back of both fragments. A ureteral catheter is then passed from the bladder up to the renal pelvis, to serve as a support while the anastomosis is being made. Directly opposite the 3 sutures serving as hinges, an axial in-

cision is now made through the center of each lip of the ends of the ureter, just long enough to permit a slight increase in the caliber of the ureter when sutured in an axial line. Between the opposite margins axially-placed interrupted sutures are now set (without penetrating the mucosa); these, when tied, will not only join the fragments in a firm union, but will increase the size of the ureteral lumen, thus taking care of a possible reduction in caliber during the healing process.

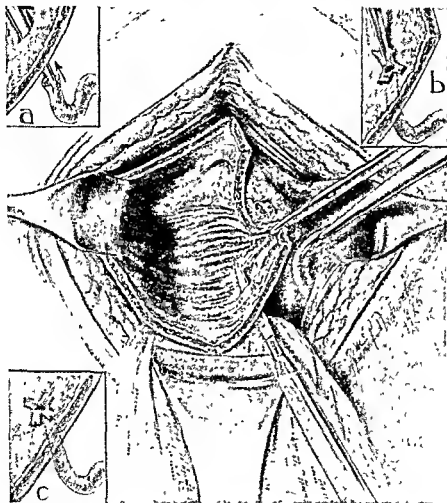
In Curtiss's method, which has been much quoted, a ureteral catheter is passed into the cut ureter and the lower end brought out through the bladder and urethra. The two ends of the ureter are sutured together, taking care that the lumen of the ureter is not penetrated by the sutures. A second ureteral catheter is passed into the ureter above the point of anastomosis through a small slit; this is passed to the renal pelvis, its purpose being to divert the urine away from its regular course. This catheter is then brought out through a stab wound in the flank. Both catheters are removed after 10 days. The use of the first catheter as a splint makes it unnecessary for the joining to be absolutely water-tight, all that is essential being coaption of both ends over the catheter with the setting in of enough fine sutures to hold them in place, since the second catheter establishes a temporary ureterostomy and keeps the urine from the raw surfaces until healing takes place.

Reimplantation into the Bladder. If the ureter can be sufficiently extended, the severed end may be reimplanted into the bladder at a point higher up on the wall. The injured ureter is exposed through a Gibson "golf-stick" incision made along the outer border of the rectus muscle, its lower end being carried across the rectus toward the midline. The origin of the ureter at the bladder is determined. The peritoneum is incised directly above the site of injury, and the ureter freed by blunt dissection from the peritoneum and connective tissue. The duct is then incised transversely, its distal end ligated, and dropped back into the abdomen.

An incision is now made through all coats of the bladder wall, in line with the ureter's original point of entrance but higher up, so that the shortened ureter can be drawn into it without undue tension. The end of the ureter may be carried through with long, very fine forceps; or it may be split for a short distance, a traction suture threaded through both fragments of the split, and carried into the bladder by a Reverdin needle. Traction on this suture draws the split end of the ureter within the blad-

der and retains it in position while the borders of the incision in the bladder wall are sutured to the ureteral wall.

Another method is to pass a catheter or bougie from the bladder side, through the incision made for the reception of the cut ureter, and into



the ureter sutured to the bladder wall.

the lumen of the detached ureter, which must be mobilized directly without. The ureter is now worked down over the instrument until its cut edge approximates the incision in the bladder wall. It is then anchored as described above.

Repair of Punctures or Incisions Involving Small Areas. Small incisions or punctures frequently heal merely by the use of an indwelling ureteral catheter, but occasionally may require suture (see *Injuries Due to Instrumentation*, p. 1315).

Postoperative Care. We have utilized most of the recognized methods of reuniting a severed ureter, and Kirwin has spent much time in experimental work upon dogs in an endeavor to discover better ways of performing this delicate and important surgical operation. Our results, however, have never justified the belief that surgical repair can restore a severed ureter to its full normal function. All patients who have had a ureteral anastomosis should receive postoperative attention for a long period. The kidney drained by the anastomosed ureter should be carefully watched and frequently tested as to its functional ability. The ureter should be dilated at intervals even if there is no immediate evidence of stricturing, as well as when a stricture has followed anastomosis, partial incision, or other incomplete injury of the ureteral wall.

Operative Treatment of Ureteral Calculus

The site of the impacted stone may be reached by several different approaches, depending upon the position it occupies.

Stone in the Upper Ureter. A stone in the upper third of the ureter may be reached by a low kidney incision, with an extraperitoneal approach to the ureter. Exposure is by the anterior half of the usual curved incision made in the loin, cutting the internal oblique muscle and splitting the transversalis along the line of its fibers. All bleeding points should be secured before the ureter is exposed, after which retractors are placed so as to protect the peritoneum, and dissection carried down to the psoas muscle, avoiding injury to the accompanying blood vessels. A tape is passed under the isolated ureter, by means of which the duct is raised sufficiently to permit the operator to locate the stone and remove it through a small longitudinal incision above its place of impaction. In cases where a stone is obstructing the ureter just below or at the ureteropelvic junction, isolation of the ureter may permit pushing the stone back into the renal pelvis, whence it may readily be removed. This approach does away with direct incision into the ureter, with its chance of consequent ureteral narrowing.

Another approach to a stone in the upper or middle third of the ureter is by an incision on the outer side of the rectus muscle, care being observed to avoid injury to the peritoneum.

Stone in the Middle or Lower Third of the Ureter. For stones located in the middle third or lower third of the ureter, the Gibson "golf-stick" incision or the suprapubic midline approach is preferable. The latter is preferred by most operators for stones in the terminal inch of the ureter. For stone impacted in the vesical end, in the male, Lowsley has devised a perineal approach, which is efficient under certain conditions. In the

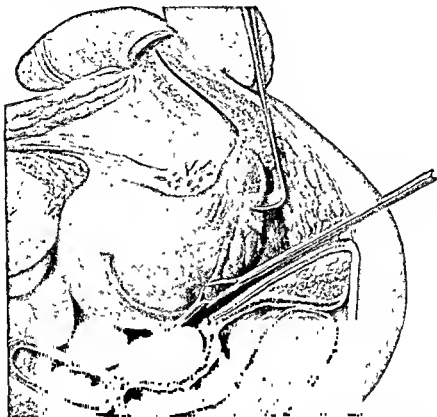


FIG. 292. Operation for removal of stone from the lower ureter of the male by the perineal route. Sagittal view, showing retraction of tissues and removal of stone from the ureter.

female, the vaginal route is employed, in certain cases, by numerous operators.

For removing a stone (or incising a stricture) the ureter must be brought into the wound enough to make it easy to incise, but it is seldom necessary to strip away much of its connective tissue. Blood vessels, in particular, should be conserved with care. A small longitudinal incision is made in the ureteral wall. Since the incision should be placed in an area not already inflamed, it usually means that the stone must be

milked up or down for a short distance. The calculus is grasped with forceps and removed. A catheter or probe is passed to the renal pelvis and then to the bladder, to make certain that there is no stricture, kink, or other stone. A single catgut stitch passed through the wall of the ureter, but not into its lumen, will close the incision. Ordinarily, an incision of this sort heals readily, but one or more Penrose drains should always be inserted down to the point of incision. After 3 or 4 days the drainage of urine through the wound ceases, and the drain may be removed.

Removal of Calculus Through the Perineum. In the male, a stone impacted in the vesical end of the ureter, which has resisted all efforts by means of cystoscopic manipulation to remove it, may sometimes be more easily extracted through the perineum than by the customary abdominal route, as suggested by Lowsley many years ago. This approach is not applicable to fat persons, nor to movable stones.

With the patient in the exaggerated lithotomy position, and a sound in the urethra, a horseshoe-shaped incision is made in the perineum, the curve being above the bulbous portion of the urethra and the ends well to each side of the rectum. The incision is deepened through the central tendon, keeping close to the urethra, as far as the apex of the prostate. Here the recto-urethralis muscle must be incised to avoid tearing into the rectum, which might result if blunt dissection were attempted. Separating the levator ani muscle from the prostate, avoiding the rectum by continued dissection upon the genito-urinary organs, the posterior surface of the prostate is exposed.

The sound is withdrawn, and a blunt-tooth retractor fixed at the base of the prostate, upon which sufficient traction is exerted to draw forward the prostate and seminal vesicles. The table, at this time, should be elevated considerably, as the wound is quite deep and the ureter is on the roof of the wound. The intervesicular fascia is then incised and drawn laterally, exposing the ampulla of the vas and the seminal vesicle of the affected side. With the rectum held down by a long, curve-backed retractor, the dissection is carried deeper, until the ureter is exposed at the point where it emerges just above the tip of the vesicle. It is isolated by blunt dissection and a tape passed around it, beyond the site of the stone if possible. By this, the ureter is drawn up into the incision, longitudinally incised, and the stone extracted. As suturing is extremely difficult at so great a depth, a cigarette drain is inserted at the point of incision, and the wound closed by drawing together the separated fibers

of the levator ani muscle, using plain catgut sutures. The outer skin is closed with silkworm gut.

Dressings should be changed frequently during the first few days, as there will be considerable leakage of urine through the wound. In order to hasten healing of the ureteral wound, a catheter may be inserted through the cystoscope and left in position for a day or two.

Vaginal Ureterolithotomy. Those who have had experience with vaginal ureterolithotomy commend it as a most satisfactory method for calculi impacted in the vesical and juxtavesical portions of the duct. The consensus of opinion is that this operation should be reserved for those cases in which the vaginal examination shows the stone to be readily palpable, and there is sufficient relaxation to permit adequate exposure. Advantages claimed for it are: (1) that it is a relatively simple method of removing a stone from a location which is frequently very difficult when other methods are employed; (2) it avoids an external incision; (3) it affords dependent drainage, should there be leakage; (4) it shortens the period of convalescence.

The operation is performed as follows: With the patient in the lithotomy position, the vagina is exposed by suitable retractors, and the cervix grasped with a tenaculum and pulled downward and to the opposite side, thus drawing down the base of the bladder and the ureter. The stone is palpated, and an incision, about an inch long, is made through the vaginal wall, in the line of the ureter. The tension on the cervix is slightly relaxed, and the index finger of the operator inserted through the incision, separating the loose tissue by gentle pressure. The ureter and its contained stone can usually be recognized as soon as the finger is introduced.

In order to prevent the migration of the stone upward along the ureter a blunt hook is placed above it, and by releasing the traction on the cervix and exerting traction gently on this hook, the ureter can be brought into the vaginal incision and the stone easily extracted through a longitudinal incision. Some operators, at this point, pass the cystoscope and insert an indwelling ureteral catheter for the purpose of preventing obstruction by any edema which may be induced. The ureteral incision may be left open, or sutured with 2 or 3 interrupted absorbable sutures passed through its outer layers. A small rubber tissue drain is placed down to the ureter, and the incision in the vaginal wall closed with a continuous suture. The drain is removed after 48 hours, and the catheter 24 hours later.

Preoperative Roentgenography. Operating-table roentgenography is of great assistance in locating a stone and in following its migrations before surgical removal is attempted. Repeated x-ray examination should always precede operation in any event. More than once a stone, planned to be removed by the surgeon in the morning, has passed spontaneously the preceding night.

Ureterectomy

The ureter, at the time of nephrectomy, is usually ligated as low down as possible, the cut end cauterized with carbolic acid followed by alcohol, and its lower portion dropped back into the loin.

In certain cases of renal and ureteral tuberculosis, however, and in papillary carcinoma of the renal pelvis or ureter, complete removal of the ureter is advisable, either at the time of nephrectomy, or at a secondary operation. In the case of tumor, we now also resect or destroy by fulguration the portion of the bladder wall immediately surrounding the orifice of the involved ureter.

A method of removing the ureter is shown in figures 293 to 296.

Uretero-Intestinal Anastomosis

During the past decade the various operative procedures grouped under the general name of uretero-intestinal anastomosis, or implantation, have received wide publicity and been performed under continually widening indications, with clinical results that have established this operation as a sound surgical procedure. The purpose of transplanting the ureters into the bowel is to secure an exit for the urine, subject to control by the anal sphincter, in one who—because of congenital anomaly, accident, or disease—is unable to void by the natural route. The earliest indication was exstrophy of the bladder. In later years, diversion of the urine from the bladder has been undertaken because of intractable vesicovaginal fistula, or when disease has made disuse or removal of the bladder necessary, as in vesical malignancy or tuberculous cystitis, or when extensive traumatic injury to the bladder makes the retention of urine impossible.

History. The first transplantation of the ureters into the large bowel was done by Thomas Smith, of England, in 1878. The operation was carried out in two stages, with an 11 months' interval. The patient apparently did well after the first intervention, but, as no means of ascertaining separate kidney function was then available, the actual state

Despite this conspicuous failure, during the following two decades many further attempts were made to employ uretero-intestinal implantation for the relief of vesical exstrophy. Associated with occasional successes along this line are the names of Maydl, in Germany, who made the first successful *intrapertoneal* transplantation of the trigone, with intact ureters, into the sigmoid, thus preserving the sphincteric action of the ureteral orifices in the hope of preventing ascending infection;

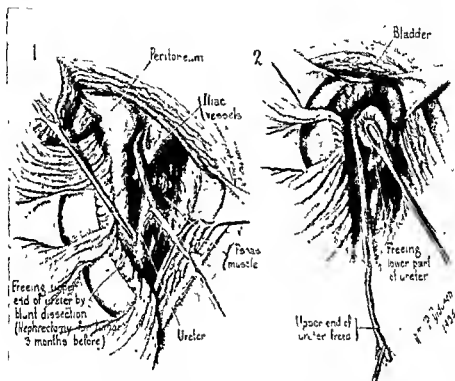


FIG 294 Ureterectomy (1) Ureter exposed. Freeing upper end of ureter by blunt dissection. (2) Freeing vesical end of ureter.

Bergenheim, in Sweden, who first utilized the principle of *extraperitoneal* transplantation into the rectum of each ureter, with a rosette of bladder wall about each orifice; Pozza, in Italy; and Peters, in Canada.

However, it was not until 1911, when Robert C. Coffey, of Portland, Oregon, presented the first of his three technics, that any satisfactory means of solving this vexing problem became available. Though others have, from time to time, offered variations and adaptations, it is the fundamental principles of *Coffey's technics* which are utilized at the

present time by most surgeons performing uretero-intestinal implantation.

In the course of animal experimentation, Coffey observed that in birds and reptiles, which have a common cloaca for both feces and urine excretion, the section of this excretory duct corresponding to the human pelvic colon was adapted for the collection of urine, while fecal material

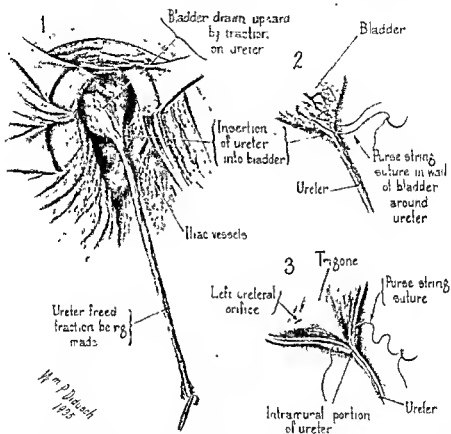


FIG. 295 Ureterectomy (1) Ureter freed down to bladder; bladder drawn upward by traction on ureter. (2) Placing purse-string suture in the wall of the bladder around the ureter. (3) Shows method of placing suture around the ureter.

regularly accumulated in another portion of the colon. Thus, the animal was able to excrete liquid and solid material separately, although both passed out through a common external orifice. Coffey, therefore, made his implantations into the pelvic colon, and in his two later technics he always adhered to this plan. It is notable that the few long-time successes now on record have been when this technic was employed.

One of Coffey's most important contributions was to emphasize the necessity for some type of **non-motile valve mechanism** at the lower end of the transplanted ureter. This he accomplished by making the ureter

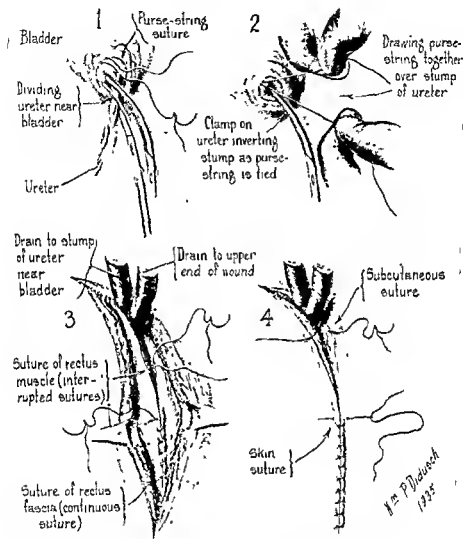


FIG. 296. Ureterectomy. (1) Dividing the ureter near the bladder. (2) Inverting the stump of the ureter as the purse-string suture is tied. (3) Suture of rectus muscle and rectus fascia. (4) Skin closure.

run immediately under the loose mucous membrane for a distance before entering the intestinal lumen. He proceeded upon the conception that the passage of the fecal current would exert pressure upon the ureteral opening in the bowel wall, thus closing it against the downward passage

of feces. This would produce a valvular effect which would minimize ascending infection. Two fundamental objections prevented the general acceptance of the operation: (1) the difficulty of preserving uninterrupted renal function while both ureters were being transplanted simultaneously, (2) the high incidence of peritonitis following the operation. Twice in the course of his researches Coffey modified his procedure to overcome these objections—the first time, by tying catheters into the ureters, which permitted bilateral transplantation without fear of ureteral obstruction; the second time, by using a transfixion suture through the ureteral wall and the mucosa of the bowel, depending upon necrosis to produce a fistula.

Prior to the introduction of Coffey's third technic, Kirwin—believing that an improvement in the operative results could be brought about if the ureteral orifices could be further removed from contact with the fecal current in the large bowel, and if some mechanism could be contrived to prevent the ascension of infection when no urine was passing down the ureter—elaborated an operation which provided an artificial tube, about 3 cm. long, intervening between the end of the transplanted ureter and the fecal current passing through the large bowel. The intention was to afford a valvular action, lessening the likelihood of infection gaining access to the lumen of the ureter. This operation, performed experimentally upon dogs, proved unsatisfactory because the canal failed to epithelialize, and a stricture eventually formed at the site of implantation, which favored, rather than retarded, the ascent of infection.

Coffey's Technics. (Technic I) The ureter is drawn into the interlamellar space immediately beneath the intestinal mucosa and its split end is dragged through an opening made in the mucosa at the caudal end of an intestinal incision and anchored inside the intestine, thereby bringing the open ureter into the intestinal lumen at the time of operation.

(Technic II) A tube or catheter is fastened within the ureter by ligatures which both seal the ureter against intestinal infection and anchor it to the catheter, after which the catheter is passed through an opening made in the mucosa at the caudal end of the intestinal incision, and is used to draw the ureter into the interlamellar space beneath the intestinal mucosa and through the opening in the mucosa into the intestinal lumen. The urine is transmitted from the upper ureter through the catheter into a receptacle outside the body. The anastomosis is completed, and the open ureter exposed to intrainstestinal pressure only after the intrainstestinal end of the ureter sloughs and permits the catheter to come away, 8 to 10 days after operation.

(Technic III) The ureter is brought into the interlamellar space outside the intestinal mucosa by an anchor stitch of chromic catgut, which fastens the end of the ureter in the angle of the caudal end of an incompletd intestinal incision. The anastomosis is gradually made by a tightly tied linen suture, which transfixes both the ureter and intestinal mucosa. The anastomosis is complete 3 to 4 days after operation.

While seemingly simple, Technic III requires certain points to make it successful. These Coffey listed as: (a) The transfixion suture must penetrate the lumen of the ureter; (b) it must penetrate the intestinal mucous membrane; (c) it must be tied sufficiently tight to finally cut through all the tissues in its bite; (d) the ligated stub end of the ureter should be anchored by a separate catgut suture to the muscular and peritoneal coats of the bowel. Technic III is especially adapted to patients having two good kidneys, such as children with exstrophy of the bladder. This technic was introduced shortly before the author's untimely death, and most of its practical applications have been by others. For patients who are to undergo cystectomy, those with vesicovaginal fistula, and adults generally, Coffey favored transplantation by Technic II, the "tube technic," because it could be done at a single sitting. Although Coffey considered Technic I outmoded by II and III, the fact that it was introduced 15 years earlier makes it still of great importance, for only by it can remote results be observed. Practically all patients operated upon more than 8 years ago, who are now available for examination, were operated upon by this technic.

Higgins' Technic. The technic of Higgins, which is a modification of Coffey's transfixion-suture method, is as follows:

With the patient in a modified Trendelenburg position, the peritoneal cavity is opened and the peritoneum incised, permitting the ureter to be dissected free from its bed so that approximately 8 cm. may be isolated. After the point of transplantation into the rectosigmoid has been selected, an incision 6.5 cm. long is made with a sharp scalpel along one of the longitudinal bands through the serosa and muscle layers to the mucous membrane of the bowel, exercising extreme care not to penetrate the mucosa so as to enter the lumen of the bowel. By lateral separation of the serosa and muscle layers, a trough is made which later will receive the mobilized ureter.

After the bowel has been returned to its normal position, the ureter is so grasped that kinking and tension are prevented when the operation is completed. The ureter is placed in the trough. One centimeter from

the lower angle of the incision in the rectosigmoid a silk suture is passed through the wall of the ureter which is in contact with the mucous membrane of the bowel. The suture is then carried through the intestinal mucous membrane as a mattress suture, and should always be put through the ureter before the bowel is entered, in order to avoid contamination. The mattress suture is tied quite tightly, after which the muscular and serous layers are drawn together over the ureter as it lies in the trough prepared for it.

The ureter is incorporated in the bowel for a distance of 2.5 to 3 cm. In this position, pressure of feces or gas passing in the bowel closes the ureter but does not interfere with ureteral peristalsis nor the passage of urine into the bladder before a uretero-intestinal fistula is formed; and when the fistula becomes established it will in no way prevent the intermittent passage of urine into the bowel.

The inner edge of the cut posterior peritoneum is stitched to the under surface of the outer edge, which is then sutured over the site of incision in the bowel that has previously been approximated over the ureter, restoring the peritoneal surfaces and placing the anastomosis behind the posterior parietal peritoneum. If this procedure appears likely to cause too great tension, the incision over the posterior parietal peritoneum should merely be drawn together, using No. 00 chromic catgut. The abdomen is closed in layers, without drainage.

Jewett's Method of Simultaneous Transplantation of the Ureters, Using a Special Electrode for Construction of the Uretero-intestinal Ostia. The electrode devised by Dr. H. J. Jewett for this operation is completely insulated except for a tiny aperture 1 cm. proximal to the tip of the beak, through which the cutting wire emerges when the lever is depressed. The cutting current thus reaches only the uretero-intestinal septum, and cannot burn the anterior ureteral wall.

The operation, which was devised by Jewett particularly for cases of cancer of the bladder, is done in two stages.

First Stage. In the first stage, aseptic intestinal beds are developed for the ureters.

The abdomen is opened through a left paramedian incision extending from just above the symphysis to the pubis. The patient is placed in the Trendelenburg position; the small intestines are packed off, and the ureters are identified crossing the iliac vessels. Each ureter is exposed by an incision through the posterior parietal peritoneum, extending from the iliac crossing downwards for 7 cm. A tape is placed around each ureter, which is gently freed throughout this distance.

That part of the sigmoid lying closest to each exposed ureter is the part selected for implantation, thus disturbing the normal relationships as little as possible.

The coils of sigmoid are lifted out of the pelvis, and the rectosigmoid held straight. It is rotated to the right so that its anterior longitudinal band lies against the exposed right ureter. The proper site along this anterior band is now selected for implantation, and an incision 5 cm. long is made through the serosa and muscularis down to the submucosa. Holding the bowel with the left hand, the edge of the lateral flap of muscularis is picked up with smooth forceps and peeled away from the submucosa for a distance of 0.5 cm. The medial flap is peeled away for only 1 or 2 mm.

Three silk traction sutures are placed in the lateral flap of muscularis, one near each end and one in the middle. These are passed beneath the ureter which is held up with tape. Traction on the sutures, with gentle pushing on the bowel, serves to slide the lateral flap beneath the ureter, which now lies comfortably upon the intestinal submucosa. The two flaps are approximated over the buried ureter with a continuous suture of 0000 chromic catgut on an atraumatic needle, but not so tightly as to squeeze the ureter at any point. The suture line is now extraperitonealized by drawing across it the lateral flap of posterior parietal peritoneum through which the ureter had been exposed. The flap is fixed to the sigmoid with 3 interrupted sutures of black silk, one just above the entrance of the ureter, one just lateral to its exit, and one midway between. The ends of the lowermost suture are left 0.5 cm. long to identify at the second stage the site of the ureteral exit.

This fixation of the sigmoid by means of the posterior peritoneum Jewett regards as one of the most important steps of the operation. The weight of the sigmoid is prevented from stretching the ureter. At the same time the ureter is made to enter and leave the bowel wall without angulation, and is extraperitonealized, except at its site of exit.

Without tension on the uppermost fixation suture, the sigmoid above the anastomosis is now swung across the pelvis to the left side. The anterior band is rotated laterally to lie alongside the exposed left ureter. The proper site along this band is selected for implantation, which is done in a similar manner with one exception. The loop of sigmoid extending between the two implantations may sag toward the right side. This will shorten the left intramural bed unless the sigmoid is anchored securely to the posterior peritoneum below the ureteral exit.

The omentum is now drawn down and the wound closed. Several stay sutures are used.

At the end of this first stage, both intact ureters lie freely in the wall of the bowel without tension, torsion, angulation, or constriction. Bringing the anterior band of sigmoid down to each ureter by producing a smooth S-shaped curve in the sigmoid preserves the blood supply and innervation by eliminating extensive mobilization of the ureters. There is no communication between the ureteral and intestinal lumens, and the position of the ureters permits the urine to flow freely into the bladder, with which they are still connected.

The ureters are now allowed to remain in their aseptic beds for at least 3 weeks before the uretero-intestinal ostia are established. During this interval a union occurs between the ureter and the enveloping bowel wall, which obliterates the undesirable periureteral space and insures collateral circulation. Intramural periureteral fibrosis, which impedes ureteral peristalsis and destroys the uretero-intestinal valve, is thus reduced to a minimum, and the future ostium is assured of a good blood supply.

Second Stage. The second stage of the operation is carried out any time after the third week. The abdomen is opened through a long, low midline incision, and the patient placed in the Trendelenburg position. The small intestines are packed off, and the sigmoid is peeled away from the parietal peritoneum until the black silk fixation sutures come into view on each side. The ends of the lowermost suture, left long at the first operation, identify the site of ureteral exit from the bowel. The emerging ureter is followed downward for 3 cm., where it is divided between clamps. The lower stump is ligated, and the upper stump is carefully freed from its investments so as to afford ample exposure of the area immediately surrounding its intestinal attachment. Excessive traction on this emerging ureteral stump must be avoided, in order to prevent any separation of the ureter from the adherent intestinal submucosa.

A purse-string suture of oiled, medium silk is now placed in the wall of the sigmoid around the emerging ureter, and left untied. Moist Mikulicz pads are placed so as to isolate everything but the elevated ureteral stump and a few centimeters of attached bowel.

This stump of ureter is held up with a clamp and split for a short distance, and the especially insulated electrode is introduced. The beak of the instrument is palpated through the wall of the sigmoid and the direc

tion of the intestinal tunnel determined. The relationship of the beak to the cutting wire is fixed in mind, and the small aperture is pressed firmly against the underlying septum a little above the center of the purse-string circle. The smallest cutting current which produces a sharp, clean incision is turned on and the wire plunged into the intestinal lumen against countertraction exerted on the ureteral stump and traction sutures. The whole instrument is quickly advanced upward about 1.5 cm., establishing a widely patent uretero-intestinal ostium, which can easily admit the tip of a curved clamp. The cut must be made directly through the septum into the intestinal lumen, and not tangentially, and must not extend so far upward as to open the ureter outside the bowel.

The ureteral stump is now amputated between a catgut ligature and a clamp, and the small, ligated end is inverted through the purse-string suture.

The same procedure is carried out on the opposite side. The peritoneum is then closed.

Total cystectomy, when indicated, is carried out at this same sitting.

The various stages of this operation are beautifully illustrated by Mr. William P. Didusch in Dr. Jewett's original presentation of the procedure (*Journal of Urology*, November, 1942).

Hutchins Extraperitoneal Method. The operation which we prefer in transplantation of the ureter is the extraperitoneal procedure devised by Doctors Amos and Ernest Hutchins, of Baltimore.

A Gibson "golf-stick" incision is made along the outer border of the rectus muscle, from a point 5 cm. above the umbilicus down to a point 5 cm. below the crest of the ilium, the lower end being turned across the rectus toward the midline. This is deepened through the fascia, muscle, and deep fascia, and the peritoneum is pushed back and retracted. The ureter is identified and isolated at its lower end. It is severed on a bevel as low down as feasible and tied, the distal end being treated with carbolic acid and alcohol.

A 3 cm. incision is then made in the peritoneum, the sigmoid identified, and a small knuckle drawn through the incision in the peritoneum. A suitable place for the anastomosis is selected and a rubber-covered clamp is applied to this part.

An incision is next made for 3.5 cm. through the muscular wall to, but not into, the submucosa of the sigmoid. The lower end of the ureter is buried in this gutter, leaving about 3 cm. of its end extending beyond the new bed. Beginning at the proximal end, the muscularis of the sigmoid

is closed over the ureter with a continuous atraumatic fine gut suture, the ureter traveling thus through the gut wall for about 4 cm.

A purse-string suture is placed into the incision in the muscularis, but not tied. A suture is inserted in the beveled end of the ureter; a small incision is made through the submucosa into the lumen at the distal end of the gutter, and the lower end of the ureter is drawn through it and fixed to the wall of the intestine, as low down as possible, by making fast the catgut suture. The purse-string suture is then pulled tight and tied.

The wall of the sigmoid is attached by a running suture of chromic No. 0 catgut on an atraumatic needle to the entire edge of the peritoneal incision, thus extraperitonealizing the area of the transplant. The entire area is then sprinkled with sulfadiazine powder. A drain is placed down to the site of the transplant and the wound is closed in layers in the customary manner.

After a suitable period of convalescence (usually 2 or 3 weeks), the opposite ureter is similarly transplanted.

Other Methods of Uretero-intestinal Anastomosis. Methods of implanting the ureters into the bowel have been devised and successfully employed by Nesbit, Hinman, Poth, Winsbury-White, Wharton, and a great many others—65 or 70 technics now being available according to a recent estimate of Wharton's. The ideal procedure has not yet been devised, however, in spite of the many improvements of recent years. The operation must still be considered a grave one, and should be undertaken only when the cure or comfort of the patient absolutely demands it.

Preoperative Preparation for Uretero-intestinal Anastomosis. The preparation of these patients for operation is of the utmost importance.

Preliminary investigation of the upper urinary tract, including renal function studies, is, of course, essential.

Chemotherapy, particularly with the sulfonamide drugs, plays an important part in preparing the urinary and intestinal tracts. For the latter purpose, sulfaguanidine may be given orally for 4 or 5 days before operation. This drug, because of its poor absorption from the gastrointestinal tract and its high bacteriostatic action against many of the bacteria which may occur there, is particularly useful in the prevention of infection in operations upon the bowel. The recommended dosage is 0.05 Gm. per kilo of body weight orally every 8 hours, day and night. Sulfaguanidine is rapidly excreted by the normal kidney.

Wharton recommends the use of sulfasuxidine in preparing the urinary and intestinal tracts for this procedure. A dose of 0.25 Gm. per kilo of

body weight is given daily for 3 to 7 days before operation. This daily dose is divided into 6 portions, given at intervals of 4 hours. Regarding the use of sulfasuxidine in the preoperative preparation of these patients, Wharton states:

Sulfasuxidine has two distinct advantages: its low toxicity, and its two-fold action on the large intestine and urinary tract. It appears to be definitely less toxic than any other sulfonamide. Also, it greatly reduces the bacterial content of the large intestine, with respect to *E. coli* and the dysentery organisms (*Shiga*, *Flexner*, *Sonne*). It is not effective against *B. typhosus*, *paratyphosus*, *alpha streptococcus fecalis* or *B. proteus*. It is also excreted in part as sulfathiazole by the kidneys, so that a urinary concentration of 50 mg. per cent is usually attained. This is a mild prophylactic dose. . . . As a urinary antiseptic, sulfasuxidine is probably not as effective as sulfathiazole and one cannot get as high level in the urinary tract. We see no reason why both should not be used together in these cases. Sulfathiazole, however, has no action on the intestinal tract.

Accompanying the sulfa drug, irrespective of which compound is used, the patient should take 1 gm. of sodium bicarbonate in order to prevent the formation of crystals in the urine, which might cause serious obstruction of the transplanted ureters.

For 48 hours prior to operation, the patient is kept on a liquid diet, and the bowel is cleaned out by means of soapsuds enemas.

Postoperative Care. Sulfonamide therapy is also very valuable after operation, in preventing infection in the intestinal and urinary tracts. It should be continued for from 7 to 10 days, in the same dosage as pre-operatively. Sulfaguanidine, as noted above, is effective in the intestinal tract but of slight value in the urinary tract; sulfasuxidine is claimed to be very effective both in the large intestine and in the urinary tract. Sulfathiazole and sulfadiazine, in conservative doses (2 Gm. a day in divided doses), are very useful in preventing and combating infection in the urinary tract. One Gm. of sodium bicarbonate should be taken in conjunction with the sulfa drug, to prevent crystallization.

Fluids should be forced after uretero-intestinal anastomosis for 3 reasons: (1) to prevent crystallization of sulfonamide in the urinary tract, (2) to relieve toxicity, and (3) to prevent urine infection. These patients should take about 3,000 cc. daily of fluids, which may be given by the most available route.

Most surgeons leave a rectal tube in position for 8 to 10 days post-operatively, a close watch being kept to see that the tube does not become obstructed by fecal matter. Keeping a rectal tube in position (1) decompresses the bowel, (2) gives information as to the amount of drainage from the kidney, and (3) prevents leakage through the anastomosis.

Remote Results of Ureteral Implantation. The increasing popularity of cystectomy, with transplantation of the ureters to the bowel, is undoubtedly due to the excellent immediate results which attended the later operations of Coffey and the work being done at present in several of the large surgical clinics throughout the United States. Of the remote results we cannot yet judge, because the marked improvements in technic are still too recent to permit sufficient periods of observation. However, patients with benign conditions who survive the operation—particularly young, otherwise healthy subjects—may be expected to live an indefinite period. It is claimed that some patients have been under observation from 10 to 15 years without showing any signs of renal sepsis (Higgins). Autopsies upon anastomosed patients, however, have almost always shown a considerable degree of urinary-tract infection and its consequences. Some patients have died as a direct result of this urinary-tract disturbance as long as 15 years after the operation was done.

Excretory urography has been of great assistance in the examination of such cases. What we are interested in is not only the immediate result, but the ultimate functional result. How well does the ureter function in its new position? What is the effect upon renal function—not one day, or a month, or even a year later—but many years thereafter? A child operated upon by Buchanan was seen in manhood by DeWitt G. Richey, suffering from a left-sided pyonephrosis and perinephritic abscess. He recovered from operation on this side, but when, 3 years later, identical pathological conditions developed upon the right side, he succumbed during the second operation. In opposition to this, Hinman saw a girl, aged 17 years, who had been subjected to intraperitoneal implantation at the age of 5 years. Excretion urography showed normal outlines for both kidneys and no evidence of ureteral dilatation on either side. *The girl was perfectly well, and carrying on the normal activities of a high school student.*

Bollinger and Walker-Taylor, of Australia, kept a dog, which had been operated upon by Coffey's "tunnel method" for almost 3 years after the operation was performed. The animal's blood urea was high for the entire period, but he appeared otherwise in good health until the last month, when he rapidly failed and died of uremic poisoning, which autopsy showed to be the direct result of the ureteral implantation.

Despite the hazards and difficulties attending the operation, and the unsatisfactory remote results, it is our opinion that ureteral implantation, properly carried out, is a most valuable procedure that has given extended

life and happiness to many. In suitable cases, where the patient's general systemic state is such as to give a reasonable hope that he can survive for any length of time, it should certainly be undertaken when indicated.

BIBLIOGRAPHY

- ALLISON, P. R.: Result of transplantation of ureters more than a quarter century after operation. *Brit. J. Surg.*, 20: 529, 1933.
- BARNES, R. W.: Management of injury to the ureter from pelvic surgery. *Urol. & Cutan. Rev.*, 411: 853, 1937.
- BEER, EDWIN: Value of ureteral implantation into the bladder and sigmoid in gynecologic injuries and diseases. *Am. J. Obst. & Gynec.*, 33: 1041, 1937.
- BIDGOOD, C. Y., AND ROBERTS, D. J.: Non-calculous obstructions at the ureteropelvic junction. *New England J. M.*, 212: 705, 1935.
- BOLLINGER, A., AND WALKER-TAYLOR, P. N.: Experimental unilateral uretero-intestinal anastomosis; 3-year survival after uretero-colostomy followed by opposite nephrectomy. *Austral. & New Zeal. J. Surg.*, 5: 268, 1936.
- BROOKS, C. D.: Bilateral nephrostomy on account of ligation of both ureters following vaginal hysterectomy. *J. Michigan State Med. Soc.*, 33: 303, 1934.
- BUCHANAN, J. J.: Remote results of bowel implantation of the ureters, etc. *Surg. Gynec. & Obst.*, 8: 146, 1909.
- CAMPBELL, M. F.: Ureteral obstruction in infancy. *Am. J. Surg.*, 5: 445, 1928.
- COBB, D. B.: Vaginal uretero-lithotomy. *Southern Surg.*, 1: 230, 1932.
- COFFEY, R. C.: Cystectomy with bilateral transplantation of the ureters in one operation. *Northwest. Med.*, 29: 443, 1930.
- COFFEY, R. C.: Transplantation of the ureters into the large intestine, etc. *Urol. & Cutan. Rev.*, 36: 637, 1932.
- COFFEY, R. C.: Further studies and experiences with transfixion suture (technic 3) for transplantation of the ureters into the large intestine. *Northwest Med.*, 32: 31, 1933.
- COFFEY, R. C.: The relative merits of 3 types of technic for submucous implantation of the ureters into the large intestine. *West. J. Surg.*, 41: 311, 1933.
- COWDEN, C. N.: A surgical accident. *Trans. South. Surg. Assoc.*, 41: 344, 1929.
- CRENSHAW, J. L., AND BUCHTEL, H. A.: Ectopic ureter with extravesical orifice. *J. Urol.*, 35: 190, 1936.
- CURTIS, A. H.: The management of ureteral injuries, with a discussion of the surgical indications in patients who require ureteral transplantation. *Surg. Gynec. & Obst.*, 48: 320, 1929.
- DAVIS, D. M.: New methods for performing ligatures of the vas deferens and for the relief of ureteral stricture. *Urol. & Cutan. Rev.*, 37: 673, 1933.
- DAY, R. V.: Ectopic opening of the ureter and heminephrectomy: 2 cases in males and 1 in female. *Urol. & Cutan. Rev.*, 36: 622, 1932.
- DEMING, C. L.: Ectopic vaginal ureter. *Surg. Gynec. & Obst.*, 62: 843, 1936.
- EISENDRATH, D. N.: Ectopic ending of the ureter. *Urol. & Cutan. Rev.*, 42: 411, 1938.
- ESTES, W. L.: Exstrophy of the urinary bladder; implantation of both ureters into the rectum; prolongation of life 24 years. *Ann. Surg.*, 99: 223, 1934.
- FARRELL, J. I., AND LYMAN, YALE: Aseptic uretero-intestinal anastomosis. *Surg. Gynec. & Obst.*, 66: 657, 1938.
- FERGUSON, CHARLES: Experimental transplantation of ureters in bowel by two stage operation, preliminary report. *Military Surg.*, 69: 181, 1931.

- FOLEY, F. E. B.: Diagnosis of anomalous renal artery as a cause of upper urinary-tract stasis. *Minnesota Med.*, 7: 359, 1924.
- FOLEY, F. E. B.: Aseptic uretero-sigmoidostomy; new roethod providing definite asepsis, etc. *Surgery*, 2: 18, 1937.
- FOLEY, F. E. B.: A new operative procedure for stricture at the ureteropelvic junction. *J. Urol.*, 38: 643, 1937.
- FOULDS, G. S.: Historical data on transplantation of ureters; Peters' operation. *Am. J. Surg.*, 22: 217, 1933.
- FOULDS, G. S., AND ROBINSON, T. A.: Late results after operation for exstrophy of the bladder. *Brit. J. Surg.*, 14: 529, 1927.
- FURNISS, H. D.: Report of the results after 12 years in a case of ureterovesical anastomosis. *Am. J. Obst. & Gynec.*, 35: 155, 1933.
- FURNISS, H. D.: Supernumerary ureters with extravescial openings. *J. Urol.*, 37: 341, 1937.
- GERAGHTY, J. T., AND FRONTZ, W. T.: A study of primary hydronephrosis. *J. Urol.*, 2: 161, 1918.
- GIBSON, T. E.: Standardization of surgical treatment for ureteropelvic obstruction. *New England J. Med.*, 222: 910, 1940.
- HARRIS, AUGUSTUS: Ureteral anomalies. . partial duplication with one branch ending blindly. *J. Urol.*, 38: 442, 1937.
- HENLINE, R. B.: The cause and treatment of non-calculous ureteropelvic obstructions. *J. Urol.*, 34: 584, 1935.
- HENLINE, R. B., AND MENNING, J. H.: The management of hydronephrosis due to ureteropelvic obstruction: preliminary report. *J. Urol.*, 50: 1, 1943.
- HENNESSEY, R. A., AND MASON, A. D.: Ureteral anastomosis. *Southern M. J.*, 23: 720, 1930.
- HERBST, R. H., AND POLKEY, H. J.: Fenger's uretero-pyelo-plastic operation: an experimental study. *J. Urol.*, 23: 23, 1930.
- HIGGINS, C. C.: Aseptic uretero-intestinal anastomosis. *Surg. Gynec. & Obst.*, 57: 359, 1933. Also: *Am. J. Surg.*, 22: 207, 1933; *Urol. & Cutan. Rev.*, 39: No 2, 1935; *Ohio State M. J.*, 32: 17, 1936.
- HIGGINS, C. C.: Cystectomy and transplantation of the ureters into the bowel for carcinoma of the bladder. *Surg. Gynec. & Obst.*, 66: 549, February 1938.
- HINMAN, F.: Result 11 years after bilateral uretero-enterostomy. *Surg. Clin. North America*, 13: 67, 1933.
- HINMAN, F.: Bilateral uretero-intestinal implantation. *Surg. Gynec. & Obst.*, 61: 801, 1935.
- HINMAN, F., AND WEYRAUCH, H. M., JR.: A critical study of the different principles of surgery which have been used in uretero-intestinal implantation. *Internat. Abst. Surg.*, 29: 313, 1937.
- HOLMES, R. J., AND COPLAN, M. M.: The management of ureteral calculi. *Southern M. J.*, 29: 673, 1936.
- HUTCHINS, E. H., AND HUTCHINS, A. F.: Exstrophy of the bladder with successful transplantation of the ureters into the bladder. report of two cases. *Surg. Gynec. & Obst.*, 36: 731, 1923.
- JEWETT, H. J.: Stenosis of the ureteropelvic juncture: congenital and acquired. *J. Urol.*, 44: 247, 1940.
- JEWETT, H. J.: Uretero-intestinal implantation: preliminary report. *J. Urol.*, 44: 223, 1940.
- JEWETT, H. J.: A new method of ureteral transplantation for cancer of the bladder. A report of 15 clinical cases. *J. Urol.*, 48: 489, 1942.

- KIRWIN, T. J.: Role of the ureter in diseases of the urinary tract. *Am. J. Surg.*, 4: 355, 1928.
- KIRWIN, T. J.: *Diseases of the Ureters*. *Cyclopedia of Medicine* (Piersol). Phila., F. A. Davis Co.
- KIRWIN, T. J.: A study of ureteral implantation, with description of a new procedure. *Am. J. Surg.*, 8: 1, 1930.
- KIRWIN, T. J.: Clinical value of experimental ureteral implantation. *Am. J. Surg.*, 23: 14, 1934.
- KUESTER, E.: Surgery of the kidneys, etc. *Deutsche Chirurgie*, 506-7, 1896-1902.
- LICHTENBERG, A. VON: Plastic surgery of the renal pelvis and ureter. *J. A. M. A.*, 93: 1706, 1929.
- LIVERMORE, G. R.: Trauma of the ureter. *Southern M. J.*, 27: 861, 1934.
- LOWER, W. E.: Vaginal lithotomy. *J. Urol.*, 14: 113, 1925.
- LOWER, W. E.: Transplantation of ureters into rectosigmoid in young children and infants: preliminary report. *J. Mt. Sinai Hosp.*, 4: 650, 1938.
- LOWSLEY, O. S.: A perineal operation for removal of stone in the lower end of the male ureter. *Surg. Gynec. & Obst.*, 32: 300, 1921.
- LUBASH, S., AND MADRID, A.: Ureteropyeloneostomy. *J. Urol.*, 38: 634, 1937.
- MARTIN, F. H.: Implantation of the ureters into the rectum; a method having for its object the making of subsequent infection of the ureters and kidneys impossible. *J. A. M. A.*, 32: 159, 1899.
- MATHÉ, C. P.: Diagnosis and present-day treatment of ureteral calculus. *J. Urol.*, 28: 133, 1933.
- MATHÉ, C. P., AND DE LA PENA, E.: Surgical repair of hydronephrosis, with reference to technical points favoring relief. *J. Urol.*, 31: 21, 1934.
- MAYDL, K.: Ueber die radikaltherapie der blasenektopie. *Wien. med. Wchnschr.*, 44: 25, 1894; 46: 28, 1896.
- MAYO, C. H., AND WALTERS, W.: Transplantation of the ureters into the rectum; end-results in 35 cases of exstrophy of the bladder. *J. A. M. A.*, 82: 624, 1924.
- MCLIVER, R. B.: Plastic surgery of the renal pelvis. *J. Urol.*, 42: 1069, 1939.
- McKENNA, C. M.: Transplantation of the ureters: preliminary report. *J. Urol.*, 19: 527, 1928.
- MOORE, T. D.: Late results of plastic surgery in hydronephrosis. *Southern M. J.*, 35: 425, 1942.
- NESBIT, R. M.: Advanced bladder and urethral tuberculosis: treatment by ureteral transplantation following preliminary colostomy. *Am. J. Surg.*, 22: 547, 1933.
- NEUSWANGER, C. H.: Uretero-ureteral anastomosis with report of case. *New Eng. J. Med.*, 215: 653, 1936.
- NORA: Une observation sur la valeur à longue échéance d'une urétéraphie. *J. d'urolog.*, 29: 501, 1930.
- O'CONNOR, V. J.: Conservative surgery in ureteropelvic obstruction; analysis of results by different techniques. *J. Urol.*, 46: 1051, 1941.
- ORMOND, J. K.: Plastic surgery of the ureter. *J. Urol.*, 25: 117, 1931.
- OTTOW, B.: Diagnosis and therapy of extravescical orifice. *Zentralbl. f. Gynäk.*, 54: 3239, 1930.
- PAPIN: Urinary incontinence from redoubled ectopic ureter; heminephrectomy. *Bull. et mém. Soc. nat. de chir.*, 59: 954, 1933.
- PATH, E. J.: An aseptic uretero-enterostomy. *Surg. Gynec. & Obst.*, 60: 875, 1935.
- PERLMANN, S.: Accessory ureter with extravescical opening in women; clinical features and treatment. *Ztschr. f. Urol.*, 23: 100, 1929.

- PETERS, G. A.: Transplantation of ureters into the rectum by an extraperitoneal method of exstrophy of the bladder. *Brit. M. J.*, 1: 1538, 1901. Also: *Canada Lancet*, 23, 1899-1900.
- POTH, E. J.: An aseptic uretero-enterostomy. *Surg. Gynec. & Obst.*, 60: 875, 1935.
- POZZA, P.: Contributo alla cura dell' estrofia di vesica. *Gazz. d. ost.* 19: 293, 1898.
- PRIESTLEY, J. T.: Conservative surgical treatment of noncalculous hydronephrosis. *Surg. Gynec. & Obst.*, 68: 832, 1939.
- QUINBY, W. C.: Plastic surgery of the renal pelvis. *J. A. M. A.*, 89: 841, 1927.
- QUINBY, W. C.: Total cystectomy for cancer of the bladder. *Ann. Surg.*, 101: 1415, 1935.
- QUINBY, W. C.: Factors influencing the operative procedure in hydronephrosis. *J. A. M. A.* 93: 1709, 1929. Also: *J. Urol.*, 38: 673, 1937.
- RANDALL, A.: Surgery of the upper ureter. *J. Urol.*, 33: 552, 1935.
- RANDALL, L. M., AND HARDWICK, R. S.: Pregnancy and parturition following bilateral transplantation for congenital exstrophy of the bladder. *Surg. Gynec. & Obst.* 58: 118, 1934.
- RICHLEY, DEW. G.: The remote sequelae of rectal implantation of the ureters for exstrophy, findings at necropsy 14 years after Bergenheim operation. *Arch. Surg.*, 11: 408, 1925.
- RITTER, J. S., AND SHIFFRIN, L. A.: Plastic surgery directed toward the relief of lower ureteral pathology. *Urol. & Cutan. Rev.*, 41: No. 8, 1937.
- SAINT, J. H., AND TURNER, G. G.: Intravenous pyelography after transplantation of the ureters. *Brit. J. Surg.*, 23: 58, 1936.
- SARGENT, O.: Basic principles covering conservative surgery for hydronephrosis. *J. Urol.*, 49: 323, 1943.
- SCHROEDER, K.: Diagnosis and therapy of ureters with extravescical openings. *Zentralbl. f. Gynak.*, 55: 868, 1931.
- SCHWYZER, A.: New pyelo-ureteral plastic for hydronephrosis. *South. Clin. North Am.*, 3: 1441, 1923.
- SHAW, E. C.: Vaginal uretero-lithotomy. *J. Urol.*, 35: 289, 1936.
- SHAW, E. C.: Perineal and vaginal cystectomy with transplantation of the ureters. *J. Urol.* 37: 850, 1937.
- SMITH, G. G.: Plastic surgery of the kidney and ureter. *New England J. M.*, 204: 297, 1931.
- SMITH, T.: Account of an unsuccessful attempt to treat extroversion of the bladder by a new operation. *St Bartholomew's Hosp. Rpts.*, 15: 29, 1879.
- STEVENS, A. R.: Longevity following uretero-intestinal anastomosis. *J. Urol.*, 46: 57, 1941.
- VERMOOTEN, V.: Transplantation of the lower end of the dog's ureter: An experimental study. II. The pathologic changes in the ureter and kidney before the end of the second postoperative month. *J. Urol.*, 32: 266, 1934.
- VERMOOTEN, V.: Transplantation of lower end of dog's ureter, experimental study. III. The function of the uretero-rectal valve. *J. Urol.*, 32: 273, 1934.
- VERMOOTEN, V., SPIES, J. W., AND NEUSWANGER, C. H.: Transplantation of the lower end of the dog's ureter: an experimental study. I. Reimplantation into the bladder. *J. Urol.* 32: 261, 1934.
- VIANNAY, CHARLES: Observation à longue échéance d'une section opératoire de l'urété suivie de suture. *Bull. et mém. Soc. franc. d'uról.*, p. 170, April 16, 1934.
- VORMANN, B.: Quoted by Harris.
- VOSE, S. N.: Hydronephrosis due to subepithelial fibrosis; treatment by adaptation Rammstedt's technic. *New England J. M.*, 210: 786, 1934.
- WADE, HENRY: The expectancy of life after ureteral transplantation. *Edinburgh M. J.* 46: 61, February 1939.

- WALTERS, W.: Transplantation of the ureters to the sigmoid colon, etc. (unilateral versus simultaneous bilateral transplantation). *Proc. Staff Meet. Mayo Clin.*, 7: 470, 1932.
- WALTERS, W.: *The conservative treatment of hydronephrosis by resection of the renal pelvis and other plastic operations.* *J. Urol.*, 29: 121, 1933.
- WALTERS, W., AND BRAASCH, W. F.: Ureteral transplantation to recto-sigmoid for exstrophy of the bladder, complete epispadias, and other urethral abnormalities with total urinary incontinence. *Am. J. Surg.*, 23: 255, 1934.
- WHARTON, L. R.: Uretero-intestinal anastomosis. Implantation of double ureter. Technique. End result. *J. Urol.*, 48: 474, 1942.
- WILDBOLZ, HANS: Dauererfolge organerhaltender plastischer operationen bei hydronephrose. *Ztschr. f. Urol. Chir.*, 31: 63, 1930-31.
- WINSBURY-WHITE, H. P.: A new method of implanting ureters into the bowel. *Proc. Roy. Soc. Med.*, 26 (No. 2): 1214, 1933.
- WODHAUS, R. P., AND CAROBBA, V.: Electro-surgical aseptic intestinal anastomosis. *Surg. Gynec. & Obst.*, 60: 1032, 1935.
- YOUNG, H. H.: Obstructions of the ureter produced by aberrant blood vessels; a plastic repair without ligation of vessels or transplantation of ureters. *Surg. Gynec. & Obst.*, 54: 26, 1932.



CHAPTER XXXVI

EMBRYOLOGY, ANATOMY, ANOMALIES, AND PHYSIOLOGY OF THE KIDNEY

A. EMBRYOLOGY OF THE KIDNEY

Three successive sets of excretory organs develop during embryological life: the *pronephros*, *mesonephros*, and *metanephros*. These, however, are not distinct entities, but are progressing generations of development of one and the same organ. All three kidneys are aggregates of uriferous tubules, which arise from the mesoderm of the intermediate cell mass (nephrotome) and show, more or less, the same structural plan. The pronephros is functional in the larval stage of amphibia and fish, the mesonephros being the permanent kidney of these animals. In man, the pronephros and mesonephros are transient, and degenerate except for a small portion of the latter, which is taken up in the development of the genital apparatus. The metanephros develops in part from the mesonephros and in part as an independent organ, and persists as the permanent kidney in man.

The Pronephros. The pronephros in man is transitory. It consists of about 7 pairs of pronephric tubules, which have their origin as solid buddings from the dorsal surface of the nephrotomes of the seventh to the fourteenth primitive segmental stalks. From each evagination a cord of cells grows dorsolaterally toward the ectoderm of the body wall. This solid cord subsequently hollows out. As it approaches the ectoderm, it turns caudad, and, reaching a similar outgrowth from the nephrotome of the succeeding segmental stalk, fuses with it. By this fusion there is formed on each side a longitudinal collecting duct—the *pronephric* (wolffian) *duct*, which extends the entire length of the embryonic body cavity and is connected with each primitive segmental stalk by a transverse *pronephric tubule*. One end of each pronephric tubule, therefore, opens into the collecting duct, while the other opens into the primitive coelom. These tubules of the various segments do not appear simultaneously, but are formed in craniocaudal sequence. The earliest tubules begin to degenerate before the last in the series appear.

Starting from the collecting duct, each fully developed pronephric

tubule is made up of a *principle tubule*, an internal *pronephric chamber*, and a *nephrostome*—the ciliated opening into the coelom. Mesial to each nephrostome a glomerulus projects into the coelom; this, lying outside the tubule, is called an *external glomerulus*. The afferent branches of the glomeruli arise from the dorsal aorta.

No pronephric tubules are developed caudal to the fourteenth segment; but the free end of the collecting duct, by a process of growth at its termination, extends caudad beneath the ectoderm, taking a direction lateral to the nephrogenic cord. As growth continues, the collecting duct eventually reaches the cloaca and pierces its lateral wall. Thus are formed the paired primary excretory ducts, at this time called the *pronephric ducts*.

Pronephric tubules have been found in embryos of 1.7 mm. length, with 9 or 10 primitive segments. In embryos of 2.5 mm., all the tubules have developed and have united to form the primary collecting duct. At a length of 4.5 mm., the collecting duct has reached the wall of the cloaca, and at 6 mm. will usually have penetrated it. All the pronephric tubules have degenerated by the 5 mm. stage, degeneration occurring in a craniocaudal direction.

The pronephric duct persists, and its caudal portion becomes the duct of the mesonephros, or second fetal kidney.

The Mesonephros. The mesonephros (wolffian body) is larger than the pronephros and located farther caudad. While it resembles the pronephros in that it consists of a series of tubules each of which at one end is related to a knot of blood vessels and at the other end opens into the primary excretory duct (now known as the *mesonephric duct*), it differs from it in four important particulars: (1) The glomerulus indents one end of the mesonephric tubule, and excreta from the blood pass directly into its lumen; (2) the nephrostomes are transitory and never open into the mesonephric chamber; (3) there is more than one tubule to a segment; (4) the tubule is differentiated into secretory and collecting portions.

The *mesonephric tubules* arise, with little or no segmental arrangement, from evaginations of the nephrogenic cord, caudad to the pronephric tubules. Two or three, or even more, correspond to the extent of a single segment. The first tubule primordia are present in embryos of 2.5 mm. length, in segments 13, 14, and 15. These hollow out, and from the lateral surface of each vesicle a solid cord of cells grows out to meet the pronephric (mesonephric) duct, which lies lateral to the nephrogenic cord.

These solid cords gradually canalize and become S-shaped. In the meanwhile, the free vesicular end of the tubule enlarges, becomes thin-walled, and forms *Bowman's capsule*, which is indented by a knot of arteries forming a glomerulus.

A complete mesonephric tubule, therefore, consists of a *mesonephric* (malpighian) *corpuscle* (Bowman's capsule and a glomerulus) and a coiled tubule, which is differentiated into a distal *secretory* portion and a proximal *collecting* portion that connects with the mesonephric duct.

Degeneration of the first formed mesonephric tubules commences at about the 5 mm. stage. As this degeneration progresses at the cranial end, the formation of new tubules goes on caudally. At 10 mm., rapid degeneration of the tubules takes place. Of 83 pairs of mesonephric tubules which have formed, only 21 pairs remain at the 21 mm. stage.

Until the embryo is 4.5 mm. long the excretory duct has no lumen, but thereafter traces of a lumen begin to appear, and at 7 mm. length the canal has become patent throughout, so that there is free communication with the cloaca.

The *mesonephric arteries* originate when the embryo is about 5.3 mm. long. They arise from the ventro-lateral face of the aorta, whence they run into the mesonephric corpuscles, where they end in a circular enlargement. Cranially, there may be seen a single artery in each segment, or in two or three segments, but as the caudal end is approached the number of arteries increases, and as many as four may sometimes be found in a single lumbar segment. While some of these vessels degenerate, those originating between the sixteenth thoracic and the third lumbar segments persist, eventually taking their places in the permanent renal arterial system as the phrenic, suprarenal, renal, accessory renal, internal spermatic, and accessory spermatic arteries. The mesonephric vessels are also the origin of those arterial branches which extend to the lymph nodes and the sympathetic ganglia that lie in the region between the superior and inferior mesenteric arteries (Felix).

The Metanephros. The chief parts of the metanephros, or permanent kidney, are the *renal corpuscles* (glomeruli and their associated Bowman's capsules) and two sets of tubules—*secretory* and *collecting*.

Like the mesonephros, the metanephros has a two-fold origin. The collecting or afferent portion (ureter, pelvis, calyces, and collecting tubules) arises from the mesonephric duct. The secretory tubules and Bowman's capsules arise from the caudal end of the nephrogenic cord, which becomes separated from the more cranial end and is now called

the *metanephrogenic blastema*. The secretory portion, therefore, has an origin similar to that of the mesonephric tubules. Subsequently, the secretory and collecting portions unite into a continuous tubule.

Development of the Ureter, Pelvis, Calyces, and Collecting Tubules. In embryos of 4.5 to 5 mm. length, a tubular bud appears on the dorsal wall of the mesonephric duct where it bends ventrally to join the cloaca. This is the *metanephric bud* or *ureteric bud*, the anlage of the collecting system of the permanent kidney, and is the earliest primordium of the metanephros (Embryology of the Ureter, p. 1208). The ureteric bud grows at first dorsally, then cranially. Its proximal, elongated portion is the ureter, while its distal end expands into the *primitive renal pelvis*. As the ureteric bud grows cranially, it impinges upon and pushes against the metanephrogenic blastema, which forms a cap about the primitive renal pelvis. With elongation of the ureteric bud, the metanephrogenic cap is carried cranially until, at about the fifth week (13 mm. length), the entire mass lies in the mesoderm dorsal to the mesonephros, opposite the second lumbar segment. This is the definitive position of the renal pelvis. Thereafter, the kidney enlarges cranially and caudally without changing its position. The ureter elongates as the embryo grows in length.

The formation of collecting tubules of the first order begins, when the embryo is from 8 to 10 mm. long, by an outgrowing of two evaginations—a caudal and a cranial—from the primitive renal pelvis into the metanephrogenic tissue. Two more soon develop between them. By the first two, the kidney acquires its poles; the intervening two—ventral and dorsal, respectively—correspond to the middle of the renal pelvis. The distal end of each primary tubule enlarges to form an ampulla, and from the ampullae two to four secondary tubules grow out. These in turn develop ampullae from which tertiary tubules arise, and this branching process continues through the fourth month, when 12 or more generations of tubules have been developed.

During the developmental period the pelvis and the primary and secondary tubules enlarge greatly. The cranial and caudal primary tubules become the *major calyces*, and the secondary tubules opening into them form the *minor calyces*. In time, the third and fourth generations of tubules are absorbed by the walls of the minor calyces, so that the tubules of the fifth order open into the minor calyces as *papillary ducts*. The remaining generations of tubules elongate and persist as the straight *collecting tubules* found in the medulla of the adult kidney.

and also project into the cortex as the *pars radiata* (medullary rays; cortical rays). The groups of convergent tubules opening into the papillary ducts, together with the secretory portions of these tubules, constitute the *renal pyramids*, the apices of which project into the renal pelvis while their bases lie peripherally in the cortex. From 20 to 30 papillary ducts open on each renal pyramid.

Development of the Renal Cortex. The secretory or glandular portion of the kidney has its origin in a mass of mesodermal cells arising from the isolated caudal portion of the nephrogenic cord. This is called the *metanephrogenic blastema*. The cap which it forms over the ureteric bud is at first very thin, and is still further attenuated by the expansion of the ureteric bud which forms the primitive renal pelvis. Cell multiplication is so rapid, however, that the tissue soon becomes very dense.

The metanephrogenic tissue is carried peripherally by the development of the collecting tubules. With the outbudding of the four primary tubules from the primitive renal pelvis, the surrounding metanephrogenic tissue is subdivided into a similar number of parts, which envelop the ends of the tubules. As new generations of tubules form, each mass of metanephrogenic tissue increases in amount and is further subdivided into as many fragments as there are peripheral collecting tubules. In this way it forms a peripheral envelop about the ends of the branches tributary to a primary tubule. Thus are formed the *primary pyramids*, each ureteric "tree" with its metanephrogenic cap being regarded as a renal unit. The apices of the pyramids, through which the papillary ducts open into the calyces, are called *renal papillae*. Later, the primary pyramids are subdivided into secondary and tertiary pyramids. So closely are these pyramids packed together that their caps come to have the appearance of a single tissue enveloping the entire kidney. This metanephrogenic tissue forms the *renal cortex*.

Each mass of tissue, covering the tips of the tubules of a pyramid peripherally, is marked off on the surface of the kidney by grooves, differentiating the space which each pyramid occupies, and this results in a certain amount of lobulation of the surface. This lobulation may persist for several years after birth, but normally the human kidney is not lobulated in the adult, as is the case with lower vertebrates and some mammals.

The metanephrogenic tissue dips down between the pyramids toward the pelvis, forming the *renal columns* (of Bertin). The *pars radiata*, as

already explained, results from the projection into the cortex of the basal ends of the collecting tubules.

The *uriniferous tubules* take their origin from the compressed metanephrogenic tissue. At about the 13 to 20 mm. stage, the metanephrogenic tissue about the tips of the collecting tubules condenses into small spheres of cells that lie in the angle between the buds of the collecting tubules and their parent stems. One sphere is formed for each new tubule. Each spherical mass is soon transformed into a vesicle with an eccentrically placed cavity. The thick distal wall of the vesicle elongates and forms an S-shaped *secretory tubule*, which unites above with the ampulla of the corresponding collecting tubule, establishing a continuous lumen. The thin proximal wall of the vesicle becomes *Bowman's capsule*, the primordium of which arises by an invagination of the wall of the vesicle directed away from the collecting tubule.

The peculiar and definite structure and arrangement of the uriniferous tubules of the fully developed kidney are derived from this S-shaped anlage. Beginning with Bowman's capsule, each fully formed tubule contains a *proximal convoluted portion*, a *U-shaped loop (of Henle) with descending and ascending limbs*, a *connecting piece*, and a *distal convoluted portion* continuous with the collecting tubule. The slightly U-shaped middle limb of the S-shaped anlage bulges into the concavity of Bowman's capsule, which has been formed by differentiation of the lower portion of the lowest limb. The upper part of the lowest limb, by enlargement, elongation, and coiling, becomes the proximal convoluted tubule. The lower part of the middle limb forms the primitive loop of Stoerck; its base gives rise to the connecting piece; and the remainder, with the upper limb of the S, forms the distal convoluted tubule. The primitive loop of Stoerck becomes converted into Henle's loop during the fourth fetal month. It also includes a portion of the proximal convoluted tubule.

The first generation of uriniferous tubules is to be found in embryos of from 13 to 20 mm. length; the second in embryos of 20 to 30 mm.; the fifth to eighth generations in embryos of 120 to 150 mm. New-born children have from 10 to 14 generations. The formation of the uriniferous tubules is not completed at the close of fetal life, but persists into the first days of postnatal life. Children up to the third month have from 14 to 18 generations of tubules.

The *renal corpuscle* is comprised of Bowman's capsule and its contained glomerulus. The arterial invasion of the invaginated portion

of Bowman's capsule occurs at about the 28 mm. stage. At first the concavity of Bowman's capsule is shallow, but as development proceeds, the walls of the capsule grow about and enclose the arterial loops of the glomerulus, leaving only an opening sufficient for the arterioles to enter and emerge.

The *renal capsule* is a rather late development, being first distinctly differentiated at the 70 mm. stage. Although the anlage of the ureter and the outgrowing collecting tubules are initially surrounded by an envelop of connective tissue, there is no organization of this tissue into a definite capsule until the fetus has attained this length.

Rotation of the Kidneys. The kidneys grow progressively upward until their upper poles are in the region of the mid-lumbar segments. At this point they rotate on their long axes in such a way that each hilum is directed toward the median line. Certain anatomists maintain, however, that even when the kidney has reached its final position, so that its poles become truly upper and lower, the hilum remains directed toward the ventral wall of the abdomen, and that it is not until the fourth and fifth months that the hilum assumes its permanent form and position.

Development of the Permanent Renal Blood Supply. Mention has already been made of certain arteries which persist from the mesonephros to form part of the permanent renal vascular system.

Embryologists are not in accord as to the exact origin of the renal blood supply, or the manner in which it develops. In general, it is derived directly from the aorta, or, less frequently, from the suprarenal artery. Because of the clinical importance of aberrant renal blood vessels, more study and literary consideration have been given to the fetal vascular supply of the kidney than to that of any other fetal organ.

The older views are those enunciated by Broman (1906), who held that all the permanent renal vessels are survivals of the mesonephric stage of development. Bremer (1915), writing on the origin of the arteries of the kidneys and other viscera, claimed that there is an absence of specificity in the developing channels of this visceral network. Instead of being predestined to supply the intestines, the mesonephros, etc., the ultimate supply of an individual organ is governed merely by mechanical convenience. New sprouts, frequently sent out from the aortic endothelium, branch and intercommunicate, both vertically and horizontally, and from these intercommunicating channels any one of several paths may become a permanent vessel. Thus, multiple renal

arteries represent the persistence of several sprouts of the aorta, with which the spermatic and the suprarenal vessels may remain connected. Similarly, an extra renal branch of the iliac, inferior mesenteric, or middle sacral artery, or of the aorta distal to the inferior mesenteric artery (likely to occur in association with pelvic kidney), represents a persistence of the more caudal elements in the anastomosis (Anson, *et al.*).

Numerous capillaries were found by Broman in the early metanephric tissue, some of which he traced to the posterior cardinal veins, while others took origin in the *venae revehentes* of the mesonephros. This suggested the possibility of a renal portal circulation in the early metanephric stage of mammals, similar to that known to exist in adults of lower vertebrates and in the embryos of the higher orders of vertebrates.

Jeidell, studying pig embryos, confirmed the existence of an abundant capillary supply for the renal anlage, but was unable to prove a renal portal current, because she clearly saw several sources whence the renal plexus might take origin. The aorta, after giving off the right and left hypogastric arteries, continues caudal and medianward as the small sacralis median artery, which gives off, besides the usual dorsal segmental branches, (1) several ventral branches which form a plexus in the region of the ureter, cloaca, and hind-gut, and (2) a number of small lateral branches which form a plexus on the ventral surface of the scleromeres. Direct connections exist between each of these plexuses and the renal plexus. There are thus two arterial sources for the early metanephric capillary plexus—one from the inferior mesenteric artery and the other from the median sacral artery. The connections with the inferior mesenteric vein accompanying the corresponding artery at the border of the colon and the efferent wolffian body veins constitute two paths for drainage for the upper pole of the mesonephros.

These observations confirm the belief that the kidney has abundant vascular connections during its entire period of development, from the time it begins to ascend and rotate up to its definite fixation in its permanent position within the abdominal cavity.

B. ANATOMY OF THE KIDNEY

Size: Shape: Position. The kidneys are paired bean-shaped organs averaging, in the adult, 10 to 11 cm. in length, 5 to 7.5 cm. in width, and 2.8 cm. in thickness. They are situated in the posterior part of the abdominal cavity, in shallow depressions on each side of the vertebral column, behind the peritoneum. The long axis of each kidney is directed

downward and lateralward; the transverse axis backward and lateralward. Their convex lateral aspects face toward the body wall on each side, and their concave medial borders toward the vertebral column.

In the adult, the kidneys lie about 1 inch from the midline at the level of the last dorsal and the first 2 or 3 lumbar vertebrae. The left kidney usually lies as high as the upper border of the eleventh rib, while the right reaches the lower border of the eleventh rib. The upper poles of both kidneys lie in contact with the diaphragm, and during inspiration the kidneys descend about an inch. The kidneys of children lie lower than those of adults. In the female, they lie slightly lower than in the male. In both sexes, the right kidney usually is situated from 1 to 2 cm. lower than the left, being displaced slightly downward by the liver.

Anteriorly, the kidneys are partly covered by peritoneum. The left kidney is in relation to the left suprarenal gland at the upper part of the medial border. Its anterior surface is in relation with the postero-inferior surface of the stomach and with the spleen, pancreas, splenic flexure of the colon, and a portion of the small intestine. The areas in contact with the stomach, spleen, and small intestine are covered by peritoneum; the others are devoid of peritoneum.

The right kidney is in relation with the right suprarenal gland at its upper extremity. Anteriorly, it is in relation with the right lobe of the liver, the descending part of the duodenum, hepatic flexure of the colon, and, at its lowest part, with a portion of the small intestine. The areas in contact with the liver and small intestine are covered by peritoneum.

The posterior aspect of the kidney is directed backward and medialward. It is entirely devoid of peritoneum, and is held firmly against the musculature of the posterior abdominal wall.

The niche in which the kidney lies is bounded posteriorly by the quadratus lumborum muscle, medially by the psoas muscle, and laterally by the broad abdominal muscles.

The Capsule of the Kidney. In addition to its own thin, closely adherent, fibrous capsule, the kidney is invested by a firm envelop of fat and fiber. A layer of fatty tissue completely surrounds each kidney, the amount and thickness of which vary greatly in different individuals. External to the *perirenal fat* is a fascial sheath—the *perirenal fascia* (Gerota's capsule). Behind this is a considerable quantity of fat which constitutes the *pararenal fat* of the retroperitoneal space.

The perirenal fascia, unlike the adipose capsule, does not completely surround the kidney. At the lateral border of the kidney it splits into

an anterior and a posterior layer. The anterior leaf passes medialward in front of the kidney and behind the peritoneum, and joins with the corresponding leaf of the opposite side in front of the large abdominal vessels. The posterior leaf extends medialward behind the kidney and the large abdominal vessels to find an attachment on the side of the vertebral column. Above, the perirenal fascia unites with the fascia of the diaphragm, while its lower edge blends almost imperceptibly with the subperitoneal fascia. The arrangement of the perirenal fascia makes it possible for the surgeon to pass from one kidney to the other without going outside the fascia. The perirenal fascia is connected with the fibrous capsule of the kidney by numerous trabeculae, which traverse the fatty capsule.

The perirenal fascia is but little evident in early life, slight trace of it being visible before the eleventh or twelfth year; but at any age the perirenal fat may easily be distinguished from other fat by its finer texture and deeper yellow color. The fibrotic and muscular structure of the perirenal capsule, and the fact that it is but lightly attached to the surface of the kidney, give it considerable elasticity. This elasticity enables it to accommodate itself to even very sudden increases in the size of the kidney, due to changes in intrarenal tension.

The kidney is supported, and held in position, partly by means of its capsules and their fibrous attachments, and partly by the apposition of the neighboring viscera and the tone of the abdominal walls.

General Structure of the Kidney. *Hilum and Sinus Renalis.* In the center of the concave medial border of the kidney is the *hilum*, a deep longitudinal fissure which receives the renal vessels, nerves, and lymphatics, and from which the ureter emerges to pass downward. The renal vein is in front, the artery in the middle, and the ureter behind, but branches of both the vein and artery are not infrequently placed behind the ureter.

The hilum expands into a central cavity—the *sinus renalis*—which contains the upper portion of the renal pelvis, the calyces, and the branches of the renal vessels and nerves. All of these structures are embedded in a variable amount of fat, which is continuous with the fatty capsule of the kidney.

Renal Pelvis and Calyces. The pelvis, with its calyces, is in reality the expanded upper portion of the ureter which lines the sinus renalis, and in its origin and development is related to the ureter rather than to the kidney. This explains the occurrence of certain anomalies, such as

reduplication of the pelves and ureters, in connection with kidneys normal in every other respect.

The pelvis subdivides to form two, or frequently three, terminal divisions, called the *major calyces*, each of which subdivides into from two to four *minor calyces*. Into each of the minor calyces opens one, or occasionally more, of the renal papillae.

The normal renal pelvis is subject to considerable variations in size and shape. In the so-called extrarenal type of pelvis, the calyces are longer and more attenuated than in the intrarenal form. In hydro-nephrosis, the extrarenal type forms a dilated sac outside the kidney; in the intrarenal form, the dilatation is largely within the kidney.

The pelvis and calyces have a mucous lining similar to that of the ureter except over the renal papillae, which are lined by a single layer of flattened epithelium. The muscularis consists of indefinite inner and outer longitudinal fibers and a distinct circular layer continuous with that of the ureter. Muschat has described a spiral arrangement of the muscle about the minor calyces, which he assumed to have a milking effect on the tubules.

The Medulla and Cortex. The kidney proper is composed of an inner *medullary zone* and an irregular outer *cortical zone*.

The *medulla*, which is sharply differentiated from the cortex, consists of a series of striated conical masses—the *renal pyramids*—the bases of which lie peripherally in the cortex while their apices converge toward the sinus renalis, where they form papillae projecting into the interior of the minor calyces. The pyramids are composed of *Henle's loops* and the straight *collecting tubules*, the latter converging to form the *papillary ducts*, which open on the papillae. The *medullary rays* are the papillary ducts and their tributary collecting tubules, which form visible subdivisions of the medulla.

The *cortex* lies directly beneath the fibrous capsule, and contains the glomeruli and most of the convoluted tubules. It is composed of the *pars radiata*—the basal ends of the collecting tubules—and the darker-colored, intervening *pars convoluta*, composed of convoluted tubules. The portions of the cortex that dip in between the pyramids are termed the *renal columns* (of Bertin), while the portions that curve across the bases of the pyramids, from one renal column to the next, filling the space between the pyramids and the fibrous capsule, are called the *cortical arches*.

The Fibrous Capsule. The kidney is invested by a fibrous capsule,

which forms a smooth, firm covering to the organ. Immediately beneath this is a layer of fine unstriped muscular tissue.

Microscopic Structure of the Kidney. Under the microscope, the entire kidney is seen to be made up of innumerable minute tubules held together by connective tissue, which is continuous with the fibrous capsule. The connective tissue is fairly abundant above the renal corpuscles and in the region of the papillary ducts, but elsewhere is very scanty.

The Structural Unit of the Kidney. Traut (1923) endeavored to show that the kidney is made up of a great number of similar "structural units" analogous to the lobules of the liver. Each structural unit consists of urinary secretory tubules grouped about a homologous portion of the collecting-duct tree. This collecting-duct tree is composed of a system of branching tubules extending from the papillary foramen to the cortex. As previously noted, the first four orders of collecting tubules become a part of the pelvic wall, while the fifth order becomes the papillary ducts. From the papillary foramen at the tip of a papilla, to the junction of inner and outer medullary zones, the collecting-duct tree bifurcates six times. The structural unit includes the collecting ducts of the tenth order (which postnatally become greatly elongated, to make room for the elongation of Henle's loops, which extend down between them) and those of the higher (cortical) orders, together with the secretory tubules connecting with them.

Each structural unit forms a pyramidal block of tissue, with its base at the periphery and connecting at its apex with the collecting-duct tree by means of a single collecting tubule. The cortical part of each unit has collecting ducts at its center, which are surrounded by convoluted tubules and fringed by rows of glomeruli, while more glomeruli are closely packed at the sides.

It has been estimated that there are more than 120 structural units tributary to each papillary duct, and from 20 to 30 papillary ducts to each papilla.

The Renal Tubule and Renal Corpuscle. The uriniferous tubules originate in the pars convoluta and renal columns as the renal corpuscles, pursue a highly circuitous course through the cortex and medulla, and terminate at the apices of the renal pyramids.

The renal corpuscle is a small, round mass, varying in size but averaging about 0.2 mm. in diameter, and consisting of a central *glomerulus* and a membranous envelop—*Bowman's capsule*.

The *glomerulus* is a small capillary plexus held together by connective tissue. In the adult kidney it varies in diameter from 0.1 to 0.15 mm. The afferent glomerular vessel supplying this capillary network originates either from the interlobular artery or, infrequently, the arcuate artery. It usually enters the capsule at a point opposite the latter's union with the tubule. The capillary branches reunite to form the smaller efferent glomerular vessel, which emerges from the capsule alongside the afferent vessel to supply the tubules. Glomeruli are most numerous in the cortex, diminishing in number toward the medulla. They are found chiefly between the interlobular arteries, to which their afferent vessels connect them. Those originating in the arcuate arteries are often twice as large as those in the cortex. The number of glomeruli for each kidney of an adult has been variously estimated at from 3 to $4\frac{1}{2}$ millions.

Bowman's capsule, which surrounds the glomerulus, is a small sac or blind dilatation consisting of a basement membrane lined by a layer of flattened epithelial cells. At the point where the glomerular vessels enter or exit, this lining folds back over the network of convoluted capillaries with which the capsule is filled, dipping down into the clefts between the vascular loops and covering the entire surface of the glomerulus with a continuous layer of flattened cells. Between the glomerulus and the capsule there is thus left a cavity lined by a continuous layer of squamous cells.

Bowman's capsule opens through a short, constricted *neck* (lined, like the capsule, with flattened epithelium) into the first section of the uriniferous tubule—the large *proximal convoluted tubule*, which is lined by columnar cells showing rows of radially disposed granules, the inner margins of the cells being equipped with fine hairs springing from the periphery. The proximal convoluted tubule pursues a complex, tortuous course in the cortical substance for a considerable distance; then takes a *straight downward course and, entering the medullary substance*, suddenly narrows down—just below the level of its glomerulus—to form the *descending limb of Henle's loop*, which dips down into the pyramid for a variable depth. This is lined by a pavement epithelium resembling that of Bowman's capsule and the neck. Suddenly enlarging, the tubule makes a sharp bend or loop and reascends alongside the first limb of the loop, forming the *ascending limb of Henle's loop* and reentering the cortical substance. At about the level of its glomerulus, the tubule becomes dilated, irregular, and forms a second coil—the *distal convoluted tubule*. This terminates in a narrow portion, which opens into a straight col-

lecting tubule. The ascending limb of Henle and the distal convoluted tubule are lined by short columnar epithelium resembling that of the proximal convoluted portion.

The straight *collecting tubule* commences in the pars radiata of the cortex, where it receives the curved end of the distal convoluted tubule. It unites with similar collecting tubules at short intervals, so that a series of fairly large tubes pass from the bases of the cortical rays into the renal pyramids. The tubes of each pyramid converge, in the medulla, to join a central *papillary duct*, 20 to 30 of which open on the summit of a renal papilla communicating with a calyx of the renal pelvis. The collecting tubule is lined by flat cuboidal epithelium, the protoplasm being clear. In the papillary duct the cells are columnar.

Conformation of the Kidney. The surface of the kidney is smooth. Normally, there can be observed in the adult a very slight lobulation, corresponding to the underlying pyramids, the lobes being marked off by faint depressions, which correspond to the underlying renal columns (of Bertin).

Weight of the Normal Adult Kidney. As the kidney cannot be weighed *in situ*, specimens on which to base statistics are limited to autopsy specimens and occasional normal kidneys removed because of ureteral trauma. Calculations for kidney weights at different age-periods, for both sexes, have been made by E. Boyd and by Herbert Wald. In practically every age-decade the normal weight was found to be slightly greater in males than in females. This is in agreement with the sex differences observed in the normal weights of other organs. Wald found that the coefficients of correlation between the weight of both kidneys and the weights of other organs are: liver, 0.60, heart, 0.32, and spleen, 0.23. The median weight of both kidneys in the male's third decade of life was found to be about 308 Gm. The weight increases slightly through the third and fourth decades until it reaches approximately 320 Gm. Subsequently, it declines until during the eighth decade it may have lost as much as 18 per cent, being reduced to a weight of around 260 Gm.

The Renal Vasculature. The blood supply of the kidney has been the subject of extensive study by numerous investigators, the epochal contributions of Bowman (1842) and Broedel (1901), and the later studies of Lee-Brown (1924) and D. M. Morison (1926) being especially noteworthy.

Abnormalities of the blood supply to the kidney are common, and will be described in detail under Anomalies of the Kidney (p. 1382).

The Arterial System. The kidney is supplied with blood by the *renal artery*, a large branch of the abdominal aorta. At the hilum of the kidney the renal artery divides into a large anterior and a smaller posterior branch, each of which subdivides into two or more secondary divisions before entering the substance of the kidney. The sub-arteries follow a course which results in nearly three-fourths of the blood being carried to the anterior half of the kidney and only about one-fourth to the posterior half. The primary anterior branch passes into the kidney in front of the pelvis, above the ureteropelvic junction, while the primary posterior branch curves around the pelvis to enter the kidney.

The renal arteries are end arteries. Broedel has shown that the primary anterior and posterior branches of the renal artery supply approximately corresponding halves of the kidney, and that each of these vascular divisions is independent of the other. The branches from one arterial tree never cross over to the opposite half of the kidney, and there is no anastomosis between the two sets of branches—a fact of great importance to the surgeon. The axes of the posterior row of calyces indicate the plane of division between these two sets of arterial offshoots.

The branches of the main renal artery diverge as they approach the kidney pelvis, until eventually they come to lie between the calyces in close apposition to their anterior and posterior aspects. Here are given off further branches—the *interlobar arteries*—which run between the pyramids, in the renal columns, toward the capsule. In the corticomedullary zone the interlobar arteries describe a slightly convex curve as they form incomplete arches over the bases of the pyramids, whence the name by which they are here called—the *arcuate arteries*. Morison observes that the arching is not as apparent in the arterial system of individuals below middle life, but becomes more marked as age advances, especially if there be any tendency to arteriosclerosis.

From their convexities the arcuate arteries give off a series of branches called the *interlobular arteries*, and then, rapidly diminishing in size, take a sudden upward course through the cortex and themselves terminate as interlobular arteries. Occasionally, small interlobular arteries are given off from the concavities of the arcuate arteries.

The interlobular arteries give off small twigs called *afferent glomerular vessels*, each of which terminates, as previously noted, in a capillary plexus—the *glomerulus*. The loops of this network reunite to form the *efferent glomerular vessel*, which leaves Bowman's capsule at the hilum, alongside the afferent vessel. In the cortical zone the efferent vessels form plexuses about the convoluted tubules. In the corticomedullary

zone they divide into two branches: a nutrient branch to the convoluted tubules and Henle's loop, and a branch which breaks up to form the *arteriae rectae*, that pass toward the pelvis and supply the collecting tubules.

Glomeruli are most numerous in the inner portion of the cortex, diminishing in number toward the medulla and being completely lacking in the cortex corticis, which consists entirely of convoluted tubules. Except for a few that extend to the capsule, or end as direct nutrient vessels, the interlobular arteries terminate as afferent glomerular vessels, each forming a glomerulus.

In addition to the interlobular arteries, three minor types of offshoots from the arcuate vessels have been described (Morison): (1) the *vasa vasorum*—occasional small, twisted, branching vessels in intimate distribution around the parent trunk; (2) *afferent glomerular vessels* of varying lengths ending in one or more glomeruli, arising at an acute angle from the main trunk—usually from the concave aspect, but occasionally from the convex surface; (3) vessels showing only a small indefinite thickening proximal to the point where they subdivide into straight medullary branches, and giving no evidence of a glomerulus.

Aside from this last group, Morison, as well as Lee-Brown, found that the *arteriae rectae verae*, regularly described in textbooks of anatomy, do not exist. All other *arteriae rectae* arise from efferent glomerular vessels and are called *arteriae rectae spuriae*. Passing down between the straight collecting tubules, they converge and form terminal plexuses about the tubules, their loops then re-uniting to form the *venae rectae*. Lee-Brown did find two types of direct nutrient vessels, however: (1) an interlobular artery ending directly in a terminal ramification surrounding the convoluted tubules of the cortex; (2) smaller arteries which branch from the trunks of the interlobular arteries, run but a short distance, and at no point show evidence of a glomerulus. These vessels finally convey blood to the tubules, after formation of a plexus for this purpose.

The Venous System. The veins of the kidney correspond to the larger subdivisions of the arterial system—that is, there are interlobular, arcuate, and interlobar veins, as well as the *venae rectae*. The two systems differ radically, however, in one respect, namely, the veins anastomose very freely.

The central venous system of the human kidney is the *arcuate*, which receives the blood from both the cortex and medulla, passing it thence into the *interlobar veins*. The latter convey it to the *renal vein*, which

emerges from the kidney at the hilum and opens into the inferior vena cava. The left vein is longer than the right, and crosses in front of the abdominal aorta.

The stellate veins—*venae stellatae*—are part of the interlobular system, and converge just below the capsule, in the cortex corticis, in radially distributed branches. These connect with the origins of the ordinary interlobular veins by means of small anastomosing radicles, which pass downward from the convex or upper aspect of the arcuate veins. Straight vessels—*venae rectae*—are described by Morison as arising in a fine venous network around the openings of the collecting tubules at the papillae of the pyramids. They come also, at times, from the reflections of the minor calyces. In either case, after pursuing a winding course among the collecting tubules of the medulla, they eventually empty into the arcuate veins, on their under or concave surfaces, or into the bases of the interlobular veins.

The interlobar veins arise at the convergence of the arcuate veins and themselves converge to form the renal vein. There is no collecting trunk posterior to the pelvis, all the veins of the posterior half of the kidney crossing over, in the lower part of the columns of Bertin, and joining the main trunks of the anterior half before leaving the kidney.

Nerves of the Kidney. The nerve supply of the kidney is derived from the tenth, eleventh, and twelfth dorsal and the first lumbar segments of the cord. The renal plexus, which lies at either side, is derived from the celiac and aortic plexuses, and consists of both medullated and non-medullated nerve-fibers, with collections of ganglion cells. Large nerve-trunks enter the hilum along with the renal artery and its branches. Within the kidney they are subdivided in much the same manner as the arterial trunks, being broken up into finer filaments, which eventually terminate in the walls of the blood vessels and of the tubules.

The renal nerves communicate with the spermatic plexus, a fact which may explain the occurrence of testicular pain in disease of the kidney.

Lymphatics of the Kidney. Our knowledge of the lymphatic system of the kidneys is rather limited, due to the great difficulty experienced by students of histology in making satisfactory preparations for tissue study. The usual methods of dye injection are difficult and often impossible when renal tissue is being examined, and the introduction of dyes and other traceable substances in the living animal has likewise proved unsatisfactory.

The most complete exposition of the subject that has come to our atten-

tion is that of Jasienski (1935). This author emphasizes the "prodigious richness" of the "vast system of lymphatic plexuses" which the kidney presents over its entire substance. Actually, they form one continuous plexus, the components of which are disposed in every part of the gland, the minute lymph channels coming in contact with all the histological elements of the parenchyma. Jasienski emphasizes especially the "inter-tubular plexus," which, his injections showed, send out branches that intervene between the tubules but do not penetrate them at any point, merely spreading over their outer aspect. These ramifications surround the capsules of Bowman in precisely the same way. The ramifications from the intercapsular plexus appear to be finer than the lymph ducts emanating from the intertubular plexus, and can be seen running with them about the capsule, the network thus formed being more dense about the neck of the glomerulus. In attempting to inject the medullary substance, Jasienski encountered the same difficulties as his predecessors, but concluded that the glomerular plexus presented, in general, the same features as those characterizing the plexuses surrounding the collecting tubules and Bowman's capsules.

Most of the lymph chains unite before they leave the kidney, forming, at the hilum, several good-sized lymphatic trunks, which communicate with adjacent lymph nodes. Some lymphatics may also be found passing through the fibrous capsule. The lymph collectors emerging from the hilum on either side have been estimated at from 6 to 11 by Nicolesco (1930) and at from 12 to 16 by Ssysganow (1930).

The efferent vessels from the right kidney proceed from the hilum of the kidney and terminate in several of the upper nodes of the right lateral lumbar chain. The regional nodes of the left kidney are less numerous than those of the right side, and consist, for the most part, in the upper nodes of the left lumbar chain and in the nodes located on the left crus of the diaphragm. Regarding lymphatic connection between the two kidneys: Hasumi (1929) mentions possible connections between the regional nodes of the right and left kidneys through fine lymph vessels passing anterior to the aorta; Ssysganow (1930) finds the regional nodes of the two kidneys connected through secondary and tertiary nodes lying on the anterior surface of the aorta; and Alice Parker (1935) finds no direct lymphatic connection between the two kidneys, though there are distinct lymph vessels anterior to the aorta which connect the right and left lateral lumbar lymph channels.

C. ANOMALIES OF THE KIDNEY

Renal anomalies occur frequently, and are exceedingly varied in type. Despite the fact that many anomalous kidneys cause no symptoms, the amassing of data from a wide range of material has made it plain that the abnormal kidney is much more likely to be the site of disease than is the normal organ.

Types of Renal Anomalies. Congenital renal anomalies may be grouped according to whether they are of (1) number, (2) size, (3) form, or (4) position. Many fall into more than one of these categories—for example, unilateral fused kidney, with crossed ectopy. In addition, there should be included anomalies of the renal blood supply. Malformations of the renal pelvis have been discussed under Anomalies of the Ureter (p 1213).

In the following table the various types of renal anomalies are grouped under the above headings:

I. Anomalies of number

- a. Absence of both kidneys (incompatible with life)
- b. Absence of one kidney (solitary kidney)
- c. Supernumerary kidney
 1. Unilateral
 2. Bilateral

II. Anomalies of size

- a. Hypoplastic kidney
- b. Renal aplasia
- c. Hypertrophic kidney (compensatory kidney)

III. Anomalies of form

- a. Lobulated kidney (fetal kidney)
- b. Polycystic kidney
- c. Fused kidney
 1. L-shaped kidney
 2. Dumb-bell kidney
 3. Shield-shaped or ring-shaped kidney
 4. Cake kidney
 5. Disc kidney
 6. Sigmoid kidney
 7. Horseshoe kidney
 - (a) With concavity above
 - (b) With concavity below
 - (c) With duplicated pelves and ureters
 8. Crossed ectopy, with fusion (unilateral fused kidney)

IV. Anomalies of position

- a. Floating kidney
- b. Ectopic kidney
 1. Simple unilateral (non-fused)
 2. Simple bilateral
 3. Bilateral with fusion (horseshoe kidney)
 4. Crossed ectopy, with or without fusion
- c. Abnormal rotation of the kidney
 1. Incomplete rotation
 2. Excessive rotation

V. Anomalies of the renal blood vessels

- a. Anomalous arteries
- b. Anomalous veins

VI. Anomalies of the pelvis (discussed under Anomalies of the Ureter, p. 1213.)

Anomalies of Number. *Absence of Both Kidneys.* Complete anephrogenesis is very rare. As it occurs only in monstrosities and is incompatible with life, it is of little clinical interest. In a majority of cases, complete renal agenesis appears to be associated with oligohydramnios, affording presumptive evidence in favor of the view that there is a direct relationship between the production of fetal urine and the secretion of amniotic fluid.

Coen (1884) collected 33 cases of complete absence of both kidneys. Mario Raso (1937) presented a case of bilateral absence of the kidney and compiled a table containing 119 other examples, the first being that of Everhard, published in 1633. As Bates, who reported 2 cases in 1933, was able to find but 5 previously recorded authentic cases, one is led to wonder at the authenticity of some of Raso's cases. Gowar (1935) states that "about a hundred cases of bilateral anephrogenesis have been found in the literature," but adds that a large number of these were premature still births or monsters with gross bodily deformities. In Gowar's own case the fetus was born 5 days before the calculated date of confinement, and showed no structural abnormalities apart from the urogenital system, which was devoid of any traces of kidneys or ureters. The amniotic fluid was present in normal amount.

Congenital Absence of One Kidney (Solitary Kidney). A much more common and important condition is congenital absence of one kidney, by which is signified the complete lack of development of one of the paired organs. There is entire absence of nephrogenic tissue on the one side, and hence absence of the kidney, ureter, and corresponding half

of the trigone. The suprarenal gland on the agenetic side is likewise absent, which is not the case in hypoplastic kidney or renal aplasia.

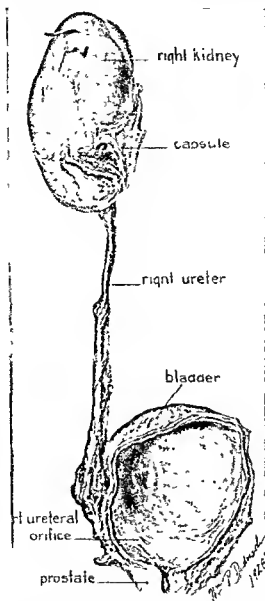


FIG. 297. Congenital absence of the kidney on the left side (solitary kidney). (Christeller.)

The solitary kidney may be found in the normal position, or in ectopic or cross ectopic position, and is characterized by a single ureter opening into the bladder and by absence of half of the trigone. It must be

differentiated from renal aplasia and hypoplastic kidney, and from the type of renal fusion in which the solitary fused organ has two pelves and two ureters opening independently into the bladder.

The recognition of unilateral solitary kidney requires careful examination, both clinically and at operation, and even at autopsy. Many authors who have reported cases of "unilateral renal agenesis" have described the presence of nephrogenic tissue in the agenetic side of the body, either in the form of an aplastic or hypoplastic mass of renal substance, or of an incomplete ureter. These, obviously, are not cases of true solitary kidney. Since most writers have failed to differentiate this condition from fused kidney, hypoplastic kidney, and renal aplasia, it is impossible to give any true idea of the frequency of its occurrence.

The complete absence of one kidney appears to be due to an arrest in the development of the nephrogenic elements of the wolffian duct, so that the "bud" or primitive nucleus of the permanent kidney fails to form. There is, therefore, absence of the corresponding half of the urinary apparatus from early embryonic life. Commonly, the müllerian duct on the agenetic side is also absent, resulting in anomalies of the genital organs—particularly in the female, in whom the genital organs are derived from the müllerian duct. The association of renal and genital anomalies has been emphasized and discussed by many authors, and has been found to be present in approximately 70 per cent of cases of congenital solitary kidney. In females, there has been seen uterus bicornis, with imperfect development of the horn of the uterus on the side corresponding to that of the missing kidney, or complete absence of the uterus or the adnexa of the corresponding side; or there may be formation of a septum in the vagina, or even complete absence of that passage. In males, absence or atrophy of the testicle, vas deferens, and seminal vesicle on the affected side has been observed. Any important anomaly of the genital tract should always suggest the probability of associated congenital absence of one kidney. Absence of the nephrogenic tissue of the wolffian duct also results in failure of the suprarenal gland to form on the agenetic side—an important point in differentiating renal agenesis from renal aplasia or hypoplastic kidney (Gutierrez).

The absence of one kidney does not incapacitate its owner for the normal physiological functions of life. The congenital solitary kidney is, however, peculiarly subject to disease, and its loss is, of course, fatal. The association of a pathological process, such as parenchymatous nephritis, stone-formation, pyelitis, and pyelonephritis, with oliguria, anuria, and death, has been frequently recorded in the literature.

With the diagnostic resources available to the modern urologist there is but slight chance of a single kidney being removed, or even operated upon, except under the most urgent of circumstances. In the past, however, such accidents were not unknown. Thomson-Walker collected 18 instances in the literature where a single kidney was surgically removed, resulting in death from uremia within a few days. The importance of utilizing the many diagnostic facilities at the urologist's disposal before nephrectomy is decided upon need hardly be emphasized.

The diagnosis of congenital solitary kidney is made by cystoscopy, the differential renal functional test, and by retrograde and excretory pyelography. By means of accurate urological and urographic examinations, it is now possible to differentiate before operation the three conditions of congenital absence of one kidney, hypoplastic kidney, and renal aplasia. The finding of a single ureteral orifice in the bladder, with a half-developed trigone, immediately suggests solitary kidney of congenital origin. However, the ureters from two normal kidneys may fuse and enter the bladder through a single orifice, or one ureter may end extravasically and another in the bladder, so that no positive diagnosis of solitary kidney can be made from vesical inspection alone, or when combined with a differential renal functional test. Roentgenograms and bilateral pyelograms are essential, and it is upon them that the urologist places his chief dependence.

The treatment of patients suffering from pathological conditions of a congenital solitary kidney must be conservative, both urologically and surgically. In cases presenting evidence of renal infection, marked oliguria, or uremic symptoms, the patient should be treated by means of renal lavage and use of the indwelling ureteral catheter, in order to secure drainage and overcome the infection. It is hardly necessary to emphasize the importance, in calculous disease or anuria of the solitary kidney, of securing adequate drainage, urologically or surgically. If operation for stone or drainage is urgently required, nephrostomy, by the ribbon-gut method, should be done, if possible, in preference to pyelostomy, because of the danger of stricture in the latter procedure.

Supernumerary Kidney. A supernumerary kidney—that is, a distinct third kidney, with independent capsule and blood supply—is one of the rarest of renal anomalies (42 cases up to 1939, Geisinger). It must be differentiated from double kidney—namely, an organ with two pelves, with or without separate ureters (*Anomalies of the Ureter*, p. 1215)—and from unilateral fused kidney (p. 1375). Many double or fused kidneys have been reported in literature as “supernumerary.”

The embryological origin of supernumerary kidney appears to be practically identical with that which we have previously cited as the cause of ureteral and pelvic duplication. At the time the ureteric bud divides prematurely (thus producing ureteral duplication), the mesenchyme, instead of covering the divided bud with a continuous envelop,

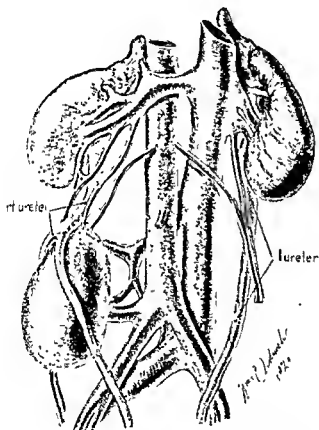


FIG. 298. *Supernumerary kidney on the right side, a very rare finding. The ureter on the right side is bifid* (Courtesy of Dr. G. S. Huntington, Columbia University Department of Anatomy)

also divides, so that each limb of the divided ureter has attached to it an independent mass of renal tissue. These two metanephrogenic masses thereafter undergo the normal developmental processes of ascent and rotation, but as two separate bodies, their courses being parallel but quite distinct. Occasionally, these two masses have been found almost equal in size and stage of development, but as a rule the extra organ is

more or less rudimentary. The aplastic and degenerated organs far outnumber those which can be considered relatively normal.

The extra kidney may be above the normal one, but usually is below it, being found at some point in the course of the ureter or lying between the ureters in front of the vertebral column. Its ureter may open into the bladder through a separate orifice, or end extravasically, or join that of the other kidney on the same side. In the last instance, the anomaly may easily be overlooked.

No symptoms can be listed as peculiar to supernumerary kidney. In only a few of the recorded cases was there any pathological condition of the anomalous organ, and even in these its involvement was generally secondary to that of the major kidney of the same side. Usually found at autopsy or operation for some unrelated condition, in very recent years urography has, in a few cases, suggested the presence of the abnormality.

The treatment of a diseased supernumerary kidney does not differ from that applicable to a normal organ.

Anomalies of Size. *The Hypoplastic Kidney.* A hypoplastic kidney is one whose development has been arrested, so that it is diminutive or infantile in size. It is to be distinguished from complete absence of the kidney, renal aplasia, and acquired atrophy. All of these conditions are of great importance, and must be taken into careful account when nephrectomy is contemplated. The relative frequency of hypoplastic kidney has been estimated at about 1 in 600.

There are two types of hypoplastic kidney. In the first, the architecture of the renal parenchyma is normal, with a normal pelvis and ureter, although the pelvis is piriform and very small and the calyces diminutive and sometimes unusually placed; in the second, the medullary portion and the pyramids are absent, so that there is only cortical substance, and the pelvis is of the hydronephrotic type (Gutierrez, 1933). Microscopic examination in some cases reveals normal kidney tissue but minimal in amount; in others, it shows rudimentary tubules and glomeruli.

In hypoplastic kidney the ureter is always patent and excretory function frequently is apparently good; but the kidney is incapable of undergoing functional hypertrophy to sustain life when disease destroys or requires the removal of its mate. The recognition of hypoplastic kidney is therefore of the greatest importance to the urologist and surgeon, and presents a fairly frequent and often difficult clinical problem.

Albarran (1902) was the first to point out the inability of the infantile kidney to undergo compensatory hypertrophy, and to warn of the danger

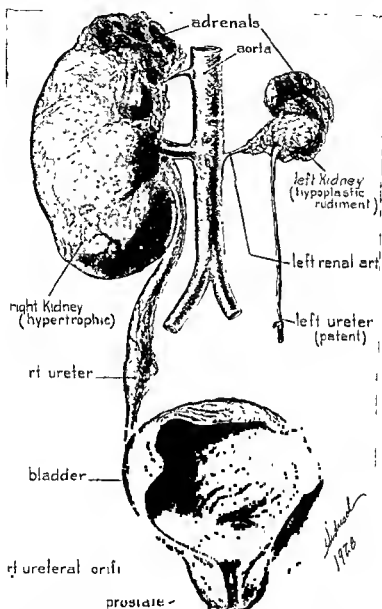


FIG. 299. Hypoplastic kidney on the left side with a hypertrophic kidney on the right. (Christeller.)

of an erroneous diagnosis because of the good elimination of urea and of color dye and the apparently good concentration of the chemical elements of the urine by many of these organs.

The diagnosis is made by relative function tests and by roentgenography. Even though the general character of the urine from the two sides may be similar, and the ability of the hypoplastic kidney to concentrate urea, etc., relatively normal, the renal function tests will invariably show subnormal function from the hypoplastic organ. However, should the kidney of the opposite side be diseased, there may be



between the ages of 12 and 13 years, she has received sanatorium treatment for pulmonary tuberculosis; x-rays, on discharge, showed no evidence of active pulmonary lesions.

diminished secretory function of both sides. Therefore, while relative functional tests are helpful, correct diagnosis is dependent upon pyelographic data.

The plain roentgenogram shows a small kidney shadow, in marked contrast with the large shadow of the kidney on the opposite side, which is always hypertrophied. Pyelography will usually reveal a very small pelvis, with the calyces absent or rudimentary; and this, in contrast with

a large normal kidney on the opposite side, will serve to verify the diagnosis. Sometimes, however, the pyelogram may show a pelvis almost normal in size. Such a pyelogram, in conjunction with a plain roentgenogram showing a small kidney shadow, will serve to diagnose the type of hypoplastic kidney with a large pelvis and a minimal amount of kidney substance. Although intravenous urograms are frequently useful



FIG. 301 Renal hypoplasia with calcified cysts. Photograph of removed specimen after the injection of 2 cc. of skiodan into the ureteral stump. The contrast medium has collected in a pouch just inferior to the upper cyst, and probably represents the renal pelvis.

in establishing the diagnosis, it cannot be too strongly emphasized that additional retrograde pyelograms are always necessary.

The treatment depends upon whether it is the hypoplastic kidney which is diseased (in which event nephrectomy is usually indicated), or whether it is the larger organ that is affected. In the latter case, the diseased kidney must be regarded precisely as though it were a solitary organ, and given the most careful treatment by urological therapy and conservative surgery.

Renal Aplasia. Renal aplasia is characterized by an arrest of embryonic development, the kidney having never been formed. The amorphous renal mass, unlike the hypoplastic kidney, has no eliminatory function, and the ureter, although opening into the bladder, has no connection with the sclerotic renal mass and is devoid of function. Histological sections made of specimens removed at operation or autopsy reveal the presence of rudimentary renal tissue characterized by embryonic and sclerotic tubules and glomeruli. Occasionally, there may



be observed a rudimentary renal artery running from the aorta to the fibrous mass of tissue. Arrest of development of one kidney is always accompanied by compensatory functional hypertrophy of its mate.

Renal aplasia, like hypoplastic kidney, must be differentiated from secondary or acquired renal atrophy. In the latter condition, the kidney undergoes complete destruction; its parenchyma degenerates and its cortical and medullary substances are lost, as in the autonephrectomy produced by renal tuberculosis, nephrolithiasis, etc. Aplasia should also be distinguished from congenital absence of one kidney, which is characterized by entire absence of nephrogenic tissue on the one side.

These patients complain merely of abdominal pain—usually on both sides of the abdomen. On the side of the aplastic kidney, this is due to the pressure on the surrounding tissue of the amorphous renal mass, which frequently undergoes partial cystic or other pathological change. On the opposite side, it is due to the enlargement of the kidney, which has undergone compensatory hypertrophy.

The importance of an accurate diagnosis, particularly when a radical operation such as nephrectomy is contemplated, is obvious, since the aplastic kidney has no eliminatory function. Cystoscopic inspection of the bladder as a rule reveals two normally placed ureteral orifices, but the ureter on the aplastic side is never patent and has no physiological function. A catheter can usually be inserted for a short distance, and opaque solution injected into the aplastic ureter will regurgitate back into the bladder. Occasionally, if there is present a rudimentary renal artery, intravenous urography may serve to establish the diagnosis; but frequently this can only be definitely made at operation.

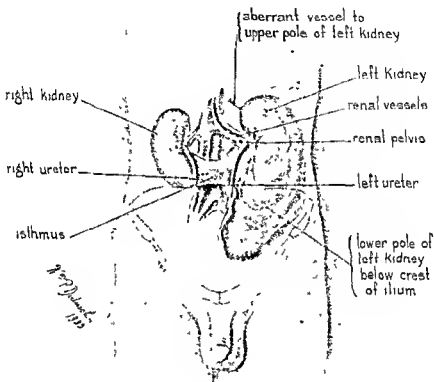
The treatment of renal aplasia, when it can be diagnosed, consists of the removal of the functionless aplastic renal mass.

The Hypertrophic or Compensatory Kidney. In cases of absence of one kidney, or unilateral renal hypoplasia or aplasia, the kidney of the opposite side will be found to be of larger size than normal, due to the fact that it has double work to do (Fig. 299). This compensatory hypertrophy will, in most cases, be evident upon examination. Therefore, whenever such examination reveals one kidney of unusual size, but apparently otherwise normal, the examiner should at once be on his guard, and any intervention upon such an organ should be undertaken only after thorough exploration of the entire urinary tract. More than once in the earlier years, before present diagnostic aids were available, a single kidney was removed, with inevitably fatal results. Even today, such an accident occasionally occurs. In these days of exquisite accuracy in urological and urographic diagnosis, operation should never be performed on either kidney without full assurance of the presence of a functioning kidney on the opposite side.

Anomalies of Form. Lobulated Kidney (Fetal Kidney). In certain mammals—for example, oxen and bears—the kidney consists of a number of distinct lobules. This lobulation is also characteristic of the kidney of the human fetus, and traces of it may persist in the adult.

Polycystic Kidney. Though of congenital origin, polycystic kidneys are better discussed under Diseases of the Kidneys (p. 1531).

Fused Kidney. The most common form of fused kidney is *horseshoe kidney*. Carlier and Gérard found 80 in 68,989 autopsies, or 1 to every 862 cases. The relative percentage, estimated from various autopsy series, has been given by others as 1 to 600 (Naumann), 1 to 1,000 (Davidsohn), 1 to 500 or 600 (Papin). We, also, found it in a proportion of about 1 to 600 in a general necropsy series.



The most common form of horseshoe kidney consists of two distinct renal organs united at the lower poles by an isthmus which may be merely a thin fibrous cord, or a tenuous membrane, or a thick mass of renal tissue which, microscopically, shows glomeruli and tubules of normal structure. Fusion at the upper poles occasionally occurs, so that the concavity is downward, but this type is much rarer. Fused kidneys lie nearer the median line than do normal ones, and are likely

to be displaced downward as well. The isthmus usually passes in front of the aorta and vena cava.

Each half of the fused kidney has its own blood supply, and several anomalous vessels are usually present. Arterial branches from the

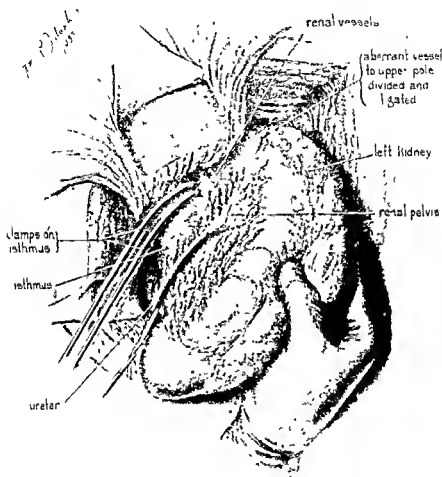


FIG. 304. Horseshoe kidney, resection of left half. Showing the kidney exposed through a lumbar incision. Clamps are applied to the isthmus. The kidney, which is very large, is about to be removed. The pathological examination showed calculus pyonephrosis, with complete loss of renal structure.

inferior mesenteric, common iliac, and external and internal iliac arteries commonly supply the fused kidney, in addition to those from the aorta.

In most cases, the ureter enters the pelvis higher up than in the non-fused organ. The frequency of hydronephrosis in horseshoe kidneys is

probably directly connected with this high insertion of the ureters, as well as with the presence of aberrant vessels. Normal rotation of the kidneys on their vertical axes is prevented by the fusion, leaving the pelves facing anteriorly or mesially; or they may face laterally and away from each other.

Asymmetrical fusion gives forms of unilateral renal fusion such as the L-shaped, shield-shaped, disc, sigmoid, cake, or dumb-bell kidney, or the fusion in crossed ectopia, which is considered separately.

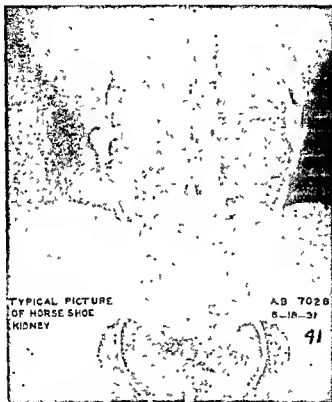


FIG. 305. Horseshoe kidney. Retrograde pyelogram.

The completely fused disc or cake kidney may also be situated in the middle line of the abdomen.

All of these forms are characterized by the presence of two corresponding pelves and two ureters, and therefore should not be confused with true solitary kidney.

The etiological factor responsible for the various forms of fused kidney is fusion of the renal fundaments in the course of their embryonic development.

Although fused kidneys may be quite normal in every respect except that they are united, such kidneys are much more liable to disease than

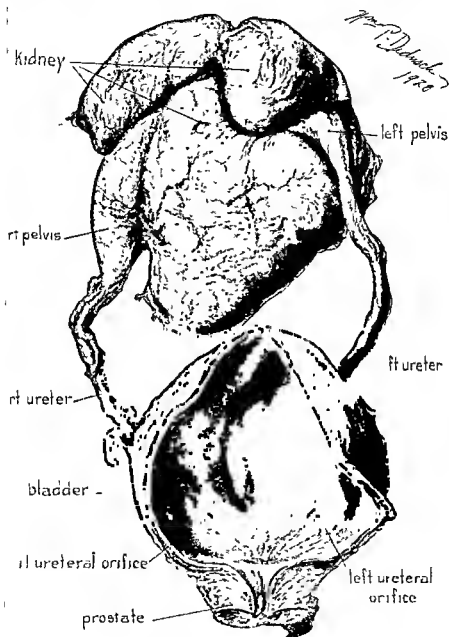


FIG. 306. Asymmetrical fusion—"cake" kidney. (Christeller.)

non-fused organs. Almost every known type of pathology has been found in fused kidneys—infections, tumor, tuberculosis, calculus, and,

most frequent of all, obstructive changes (hydronephrosis). Because of its susceptibility to disease, as well as its relatively frequent occurrence, the fused kidney presents a clinical problem of great importance.

Pain in the epigastric or umbilical region, gastrointestinal disorders, and recurrent urinary disturbances are present in a very high percentage of cases of horseshoe kidney. If complications involve one half of a symmetrically lying horseshoe kidney, the pain may be more lateral than median; but if the position of the kidney is one-sided, and the lower-lying pole is the diseased portion—which is likely to be the case—the pain will be median.

Although urography has facilitated the discovery of all types of renal anomalies, including fused kidneys, failure of preoperative recognition of horseshoe kidney is still a common occurrence. In the New York Hospital's series of 25 cases (up to 1932) every one of the patients had been examined at other clinics or by supposedly competent physicians. Twelve of them had been operated upon for relief of symptoms apparently due to the anomalous renal arrangement, the diagnoses being chronic appendicitis, cholecystitis, cholelithiasis, and other intra-abdominal conditions unconnected with the kidneys. Intravenous urography and other advances in urological diagnostic precision have greatly aided in the recognition of fused kidney, and a complete urological examination should now result in accurate preoperative diagnosis in most cases.

Although the final decision must rest on the interpretation of the x-ray pictures, the physical examination may be of considerable importance. Occasionally, it has proved possible to palpate the isthmus, or a mass lying across the median abdomen, or on one side of the vertebral column.

A sign some diagnosticians have found of value is accentuation of the pulsations of the abdominal aorta, which may be discovered both by palpation and auscultation. It is due to the extra pressure that the existence of the isthmus brings to bear upon the great vessels, which are also abnormally tightened by the necessity of passing through abnormally placed tissue.

The pathological horseshoe kidney, especially if it contains stones, can sometimes be recognized in a plain x-ray film. Ureteropyelography, however, gives the most reliable evidence. The lower calyces will be seen to point centrally. Gutierrez found the most valuable pyelographic data obtained in the New York Hospital series to be: (1) inversion and rotation of the pelves; (2) unusual localization of the elongated and bizarrely shaped pelves, which are often close to the midline, frequently overlapping the vertebral column; (3) peculiar position of the ureters,

which, though they seem to come from behind, are really cephalically or ventrally situated, giving the appearance of a bottle-neck where the ureter emerges from between two calyces. (In a normal pyelogram the ureters emerge laterally and internal to their pelves.) Everted pelves, facing away from each other, are also seen. Both the retrograde and excretion methods are useful. If function in both sections is even fairly good, excretion urography will plainly show the abnormal position of the pelves and calyces and the angle at which the ureters are compelled to traverse their course between the pelves and the bladder orifices.

The treatment of acute infections (pyelitis, pyelonephritis) occurring in a fused kidney is similar to that of infection in a normally formed organ: urinary antiseptics, forced fluids, rest in bed, ureteral dilatation, and other measures designed to improve the defective drainage and detoxicate the patient as rapidly as possible. In general, once a fused kidney has become diseased there is little hope of permanent cure by anything but radical measures (Operative Treatment of Fused Kidney, p. 1689.) Though palliative treatment may temporarily clear up some conditions, recurrence is almost inevitable because of poor drainage due to the high insertion and abnormal course of the ureters.

Unilateral Fused Kidney, with Crossed Ectopy. In this type of anomaly, one kidney is displaced to the opposite side, to a point below the other organ (which is usually in normal position), the adjoining poles of the two kidneys being fused. Fusion of this type does not produce the regular "horseshoe," but is likely to result in an oval mass, or in a tandem arrangement (sigmoid kidney). The ureter from the pelvis of the upper kidney passes down to enter the bladder on the same side; that from the pelvis of the lower kidney crosses the median line and enters the bladder on the opposite side. The ureters therefore open in their normal positions on the trigone, and cystoscopy gives no hint as to the anomalous condition.

Crossed ectopy may also occur without union of the two organs, which lie close together, the ectopic kidney being the lower.

In the more common, tandem-arrangement, the ectopic kidney is likely to be smaller than usual and may be lobulated, as in the fetal state. The connections with its blood supply—i.e., the aorta and the common or external iliac arteries—will have been altered to conform to the kidney's abnormal position; but the calyces of its pelvis almost always point toward the side where the kidney should properly lie, although the pelvis itself will usually lie in an anterior position.

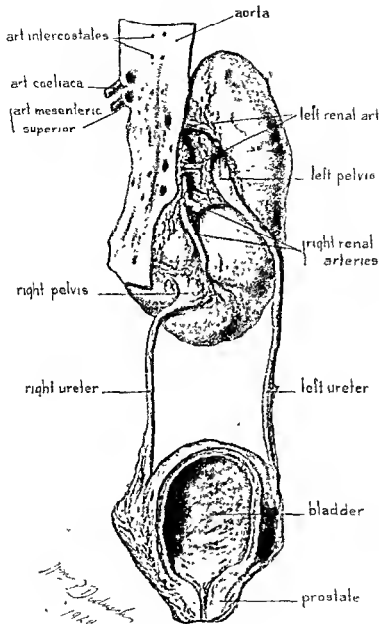


FIG. 307. Unilateral fused kidney with crossed ectopy. (Christeller.)

The displacement and the crossing of the ureter predispose to hydronephrosis, infection, lithiasis, and other pathological changes, which often require surgery.

Anomalies of Position. Ectopic Kidney. One or both kidneys may be congenitally displaced and remain fixed in this abnormal position. Displacement of one kidney to the opposite side, below its normally situated mate, with fusion of the two kidneys, is discussed above in connection with fused kidneys. Crossed ectopy may also occur without fusion. Morton M. Mayers, in 1936, published a list of 20 such cases which he had collected from the literature. We therefore have (1) simple unilateral ectopy, (2) simple bilateral ectopy, (3) bilateral ectopy with fusion, and (4) crossed ectopy, with or without fusion.

Ectopia of the kidney is due to interference with the migration of the kidney anlage (metanephros) during fetal development. Originally, the metanephros is within the bony pelvis, but about the end of the eighth week of intrauterine life it gradually shifts its position until it is opposite the position of the first four lumbar vertebrae, and has established a contact with another embryonic gland—the adrenal. During its ascent the kidney acquires a blood supply from vessels more or less temporary in character, but should circumstances retard or stop entirely its migration, these normally temporary vessels may become permanent, and fix the organ at whatever point such interference with migration may have taken place. The process of ascent and rotation may also at times be mechanically prevented because of anomaly in some adjacent organ, which forces the kidney out of its natural course. Only rarely is an ectopic kidney found *above* its normal level, and in these cases it appears probable that the fetal organ formed attachments to vessels located so high that the kidney was pulled upward because its aortic attachment was so far above the normal.

Available statistics variously place the incidence of occurrence of ectopic kidney at approximately 1 out of every 660 to 1,000 persons. Guizetti and Parisets found renal dystopia in 0.10 per cent of 9,882 male and 0.08 per cent of 10,119 female cadavers.

The range of possible displacement downward is considerable. The kidney may be found at any point between its usual location and the base of the bladder—in the iliac fossa, over the sacroiliac joint, on the promontory of the sacrum, or far down in the pelvis, in the regular course of the ureters. Mild degrees are to be differentiated from acquired renal ptosis. Upward displacement into the thoracic cavity has been reported in a few instances.

In the relatively rare cases of bilateral ectopy, fusion is common.

Alterations in the shape and size of the ectopic kidney are common.

as it cannot develop properly in its abnormal environment. Not only is it regularly smaller than normal, but it will usually be flat, ovoid, discoid, or even pyramidal in shape. It may or may not be lobulated. If the kidney rests on the promontory, or the sacroiliac joint, there will be a depression upon the posterior surface. The pelvis, in most cases, retains its embryonic (anterior) position, and, in the absence of a definite hydronephrosis, may be small or hypoplastic, often lacking complete formation of any calyces but the superior and inferior major ones. At times, over-rotation of the ectopic kidney will be in evidence, the pelvis facing posteriorly or even laterally. The ureter may be abnormally short and is frequently tortuous, although in many cases its course to the bladder is straight and unhindered. In the more common lumbar and iliac types of ectopy, a normal fatty capsule will be present, but in the rarer pelvic kidney the perirenal fat will be lacking. The kidney is anchored to surrounding structures by adhesions and aberrant vessels.

The blood vessels supplying the ectopic kidney are always anomalous. One of the chief anatomical differences between acquired renal ptosis and ectopic kidney is the fact that the vessels, in ectopia, are given off much lower down on the aorta and are more plentiful. If the kidney lies over the sacrum, or in the bony pelvis, it may receive branches from the iliacs, the middle sacral, or the inferior mesenteric arteries. If displaced far to the left, the major arterial supply may come in from the right; or the process may be reversed, in case of right-sided displacement. The great vessels are usually accompanied by individual veins, but cases have been reported of a single large vein taking care of the return flow from three or four arteries.

An ectopic kidney usually gives no symptoms unless it is diseased. As a rule, however, such kidneys drain defectively, and are poorly nourished, due to the inefficiency of the anomalous vessels which provide their blood supply. In addition, they are likely to be injured, and their function interfered with, by pressure exerted upon them by adjacent structures. The normally placed opposite kidney generally presents some degree of compensatory functional hypertrophy. Interference with its drainage predisposes the ectopic kidney to infection, and it is infection that usually brings these patients to the physician.

Although ectopic kidneys occur with about the same frequency in male and female patients, clinical symptoms of this condition—most often pain in the pelvis or lower abdomen—are more common in the latter sex. Such symptoms have frequently been mistakenly attributed to

the generative organs; and in both sexes, obscure abdominal symptoms due to an ectopic kidney may be erroneously referred to the appendix.

The diagnosis of ectopic kidney is readily made by retrograde pyelography or excretion urography. Shortness of the ureter, as revealed in the pyelogram or when inserting a catheter in the retrograde method, should at once suggest an ectopic kidney of the pelvic type.

Surgery in an ectopic kidney is often necessary, and is discussed under Operative Treatment of Ectopic Kidney (p. 1694). Other cases may be successfully treated by diet, urinary antiseptics, and ureteral dilatation with renal pelvic lavage.

Abnormal Rotation of the Kidney. Anomalous rotation of fused, ectopic, or otherwise malformed kidneys is, as we have seen, common; but there may also be abnormal rotation of kidneys which are otherwise normal.

In the course of the kidney's development, it undergoes an upward migration, as well as a rotation around its longitudinal axis. If this rotation is *incomplete*, or fails to take place, the renal pelvis and hilum will remain in an anterior position. If the rotation is *excessive*, the pelvis and ureter will descend behind the kidney or along its external border. Whether incomplete or excessive, the anomalous rotation may cause obstructive changes, necessitating plastic operation, nephropexy, or even nephrectomy.

Anomalies of the Renal Blood Vessels. Accessory or aberrant blood vessels to the normally placed kidney are common and of great variety. They are of importance to the surgeon because they increase the hazards of operative work upon the kidney, and to the clinician because of the frequency with which they cause, or help to cause, hydronephrosis.

In congenitally misplaced kidneys, as previously noted, the blood supply is always abnormal, being derived from the nearest arterial source.

The first important observations on this subject were published by the Anatomical Societies of Great Britain and Ireland in 1891. Eighteen years later, Seldowitsch, a German investigator, examined 300 kidneys which he had dissected with a view to determining how frequent is the occurrence of abnormal renal vessels. In 1920, D. N. Eisendrath published the results of his exhaustive studies upon the subject, and, although much has been written since, later investigators have added little of importance to Eisendrath's description of the anatomical variations commonly encountered.

Arteries. Anomalous arteries extending to the upper and lower poles

are the most frequently met with. These may arise from the aorta, the renal artery, or from other arteries such as the common and internal iliacs, spermatic, middle sacral, hepatic, and inferior mesenteric. There may also be duplication of the main renal artery; or the right and left renal arteries may both arise from a single aortic trunk.

An upper polar artery arising from the main renal artery is usually short, taking its origin from the main renal artery at a point just before that at which the latter enters the hilum. It may, however, arise further back, nearer the aorta—so close, in fact, that for all surgical purposes it has the same significance as one arising directly from the aorta.

Upper polar arteries from the aorta usually enter the kidney at its mesial border—rarely upon the anterior or posterior surfaces. Usually there is but one such artery, but occasionally a superior polar artery to each kidney will be observed.

Lower polar arteries from the main renal artery are uncommon.

Lower polar arteries from the aorta are of great importance as they may compress the ureter and cause hydronephrosis. They also stand in danger of being injured during operations upon the kidney. Such inferior polar arteries not infrequently occur on both sides, either singly or in pairs; and either of these pairs of anomalous vessels may be accompanied by a corresponding inferior polar vein.

Lower polar arteries arising from the common and internal iliacs, middle sacral, or inferior mesenteric arteries are occasionally encountered.

Duplication of the main renal artery is sometimes seen. The two arteries may be so far apart that one of them may be mistaken for an accessory artery to the lower pole.

It has been determined that upper pole arteries arising from the main renal artery occur in about 1 out of 200 kidneys; upper polars arising from the aorta in about 1 out of 190 kidneys; and lower polars from the main renal, the aorta, or the iliacs, middle sacral, or inferior mesenteric arteries in about 1 out of 185 kidneys.

The retropelvic artery is usually represented as having a fan-like distribution, but dissections have shown many variations of this arrangement. The pelvis may be crossed by one or more anomalous vessels of large size, or even by the main renal. The commonly accepted course of the main retropelvic artery is called by Eisendrath the *high type*, to distinguish it from (a) a high middle and low or fan-like distribution, (b) a high and middle type of branching, (c) a high and low type, (d) a single artery crossing the center of the pelvis, and (e) a middle and low

type, each of which he found 2 or more times in 124 dissections. Division of the single main renal artery into equal-sized branches is a common finding. Where there are two main renal arteries, one frequently becomes the retropelvic, taking its origin directly from the aorta instead of from the main renal artery.

Veins. Abnormalities of the renal veins are much less frequent than anomalies of the arterial system. Normally, there is one anterior renal vein. Anomalous arrangements vary considerably. The main renal vein may divide into branches of equal size, which pass before and behind the pelvis. The main renal vein, instead of being prepelvic, may be retropelvic—an arrangement found in over 4 per cent of kidneys. Aberrant veins from the upper and lower poles occur. A large vein directly from the vena cava and an artery directly from the aorta have been found crossing in back of the pelvis.

D. PHYSIOLOGY OF THE KIDNEY

The function of the kidney, broadly considered, has been defined as "the maintenance of that constancy of composition of the internal fluid environment of the cells of the body which is essential not only for health but for survival." (Richards, 1938) This function, which it shares with the skin, the gastrointestinal tract, and the respiratory system, it accomplishes by the elimination of urine. Not only must it rid the body of useless and harmful substances, such as unrequired water and salts, the waste products of metabolism, and foreign substances, but it also must protect the body against the loss of substances necessary for its maintenance—water, inorganic bases essential for the electrolyte balance of the blood, and diffusible food-stuffs.

Although the literature contains voluminous accounts of experimental researches regarding the range of activities of the kidney—researches which have given rise to the many diagnostic and prognostic tests of renal function now available—these studies have yielded little information which defines the exact processes by which urine is formed within the kidney. The relating of secretory or conservatory processes to the different parts of the renal apparatus remains, to a considerable extent, hypothetical. In spite of the great progress toward their solution that has been made in the last quarter century, the same questions which troubled the physiologists of the eighteenth and nineteenth centuries are still of great concern to present-day students of renal function, namely: (1) the extent of the glomerulus' participation in the formation

of urine, and whether its role is an active or a passive one; (2) whether the tubule cells secrete substances from the blood into the lumen of the tubule, or whether they secrete constituents of the glomerular urine back into the blood from the lumen of the tubule, or whether they do both; (3) whether the structurally different portions of the tubule have different functions.

Earlier Concepts. Laurentio Bellini is believed to have been the first to publish a description of the renal tubules. In 1662, at the age of 19 years, he wrote a book called *De structura renum*, based on dissection of the kidneys of a deer; in this was noted, for the first time, that the kidney "meat" was in reality a mass of tiny tubes, which arose from all directions but discharged their contents through a common outlet, the renal pelvis.

In 1666, Malpighi described the globular bodies in the cortex, which soon became known as the malpighian corpuscles. He showed that they were connected with the arteries, but was unable to demonstrate their connection with the tubules, although he surmised it.

In 1842, William Bowman, a young English anatomist and a master of dissection, published the results of his studies of the complicated structure of the renal tissue and the arrangement and function of the renal blood supply. More than 175 years after Malpighi's demonstration of the renal corpuscles and their connection with the arteries, Bowman showed that each of these globular bodies is the dilated extension of a urine-bearing tubule and forms a capsule about the arteries, the intracapsular space being continuous with the lumen of the tubule. He was thus the first to demonstrate the renal unit. Having noted a resemblance of the renal tubules to the acini of the digestive glands, Bowman concluded that the tubule cells secrete the waste products of metabolism from blood, and that these are washed out of the lumina by a saline stream which escapes from the blood through the glomerular capillaries.

Shortly thereafter (1844), Carl Ludwig made known his hypothetical conception of Bowman's capsule as a simple filter, which permits all the blood-plasma constituents except proteins to pass through it. In its passage down the renal tubule this filtrate is elaborated into urine, being concentrated and reduced in volume by reabsorption of much of the fluid from the tubule to the blood. Ludwig's theory was one of simple filtration and reabsorption, in no way dependent for its continuance upon any vital capacity of the constituent cells. It had widespread acceptance for many years.

The work of Heidenhain, of Breslau (1874-1884), caused a return to

the secretory theory originally advanced by Bowman. But, whereas Bowman regarded the tubule cells as secretory because of their appearance, Heidenhain conceived them as secretory because his investigations appeared to show that the diffusible dye, indigo-carmin, injected intravenously, is excreted in the urine in high concentration, but sections of the kidney made during its excretion showed no evidence of its presence in the glomerular capsule. Further investigations showed massive accumulations of indigo-carmin within the lumina of the tubules under experimental conditions which Heidenhain believed abolished glomerular function entirely. This investigator concluded, from his skilfully conducted studies: (1) that the glomerulus is not a filter but a secreting structure with the capacity of selecting what shall pass through it, (2) that the cells of the renal tubules are secreting cells, (3) that the rate of blood flow through the glomerular capillaries, rather than the blood pressure within them, is the prime factor in the production of glomerular urine.

The Bowman-Heidenhain secretory theory held sway until the beginning of the present century, when there began to take place a gradual return to belief in the filtration doctrine.

In 1917, Cushny, after a thorough analysis of the voluminous literature dealing with the two theories of secretion and filtration-absorption, extended Ludwig's views into what is termed the "modern theory" of renal function. The chief points in this theory are:

(1) The blood pressure in the glomerular capillaries suffices for filtration, and the capsule filters off the colloidal substances of the blood plasma to which it is impermeable, while allowing the rest of the constituents to pass through without alteration in their relative concentrations. The glomerular filtrate is thus practically deproteinized plasma.

(2) In its passage through the tubules, this fluid is altered by the absorption of certain of its constituents by the epithelium. The passage of the absorbed water and solids is an active absorption—not the passive diffusion believed by Ludwig to be sufficient.

Current Beliefs. In the two decades which have elapsed since Cushny summed up the "modern theory," great progress has been made in our understanding of the internal mechanisms of the kidney.

Due largely to the work of A. N. Richards and his colleagues at the University of Pennsylvania, the existence of glomerular filtration and tubular reabsorption has been positively demonstrated. These investigators adapted to the study of the kidney two technics used in other con-

nections by other workers. One was a method of microscopic observation of the frog's kidney during life. The other was a micro-dissection method of obtaining samples of the fluids from the glomerulus and parts of the tubules, so that they were able to make chemical analyses of these minute quantities of fluid for the determination of individual constituents. They found that glomerular urine collected from frogs had the same composition as a plasma ultrafiltrate with respect to total concentration of solutes, total electrolytes, pH, chlorides, inorganic phosphates, glucose, urea, uric acid, creatinine, phenol red, indigo-carmin, and polysaccharide inulin (the last five substances having been injected intravenously or subcutaneously before the collection of the glomerular urine).

"These results," says Richards, "seem to me to leave little room for doubt that, in amphibia, the glomerular urine actually has the composition of a protein-free filtrate from plasma, precisely as Ludwig had imagined 93 years ago. They show that, so far as the frog is concerned, Heidenhain was wrong in denying that indigo-carmin escapes from the blood through the glomerular membrane. They give no evidence that the glomerulus possesses any capacity whatever of selecting what substances shall or shall not pass through it if only they are diffusible."

Subsequent investigations by Richards and others have convinced most students of renal physiology that the conclusions drawn from amphibian experiments that the glomerular process is one of filtration can be safely applied to mammalian and human glomeruli.

The fact that inulin, despite its high molecular weight and low diffusibility passes through the glomerular membrane as rapidly as do the much smaller molecules of urea and glucose indicates that the glomerular membrane is a relatively wide-meshed sieve.

Inulin is excreted solely by the glomerulus, and its concentration in the glomerular urine is the same as that in the water of the blood plasma. Hence, in the *inulin test* we have an accurate method of measuring the rate at which the glomerular filtrate is formed and delivered into the proximal ends of the renal tubules. The amount of inulin excreted in the urine in a minute divided by the amount contained in 1 cc. of plasma (i.e., plasma filtrate) gives the volume of filtrate in cc. per minute. (Richards) Professor Homer W. Smith, at the New York University Medical College, has shown that for adult man under basal conditions 120 cc. per minute is the average rate at which glomerular urine is formed.

The beginning of urine formation, therefore, consists in the separation from blood "of a torrent of undifferentiated filtrate by a blind physical

force. Its volume is so great as to contain all of the normal constituents of plasma which must be excreted, with the probable exception, for man, of a fraction of the creatinine; it contains also relatively vast quantities of glucose, amino acids, and salts which must not be excreted." (Richards) This filtration is accomplished by the glomerulus and its surrounding Bowman's capsule, which, as we have seen, is the dilated extension of a uriniferous tubule, the intracapsular space being continuous with the lumen of the tubule. The blood pressure in the glomerular capillaries suffices for filtration, and the capsule filters off all the blood-plasma constituents except protein, to which it is impermeable.

However, if this filtration were uncorrected, death from dehydration and loss of bases would promptly ensue. The corrective processes by which this is prevented—namely, the reabsorption of the water, salts, and diffusible nutrients essential for survival—are distributed among the various segments of the uriniferous tubule, the secretory capacity of which is selective. The glomerular filtrate, therefore, is elaborated into urine in its passage down the renal tubule, being concentrated and reduced in volume by the active absorption of certain of its constituents by the epithelium of the tubule.

That the tubule cells also have excretory capacities has been made clear largely through the work of E. K. Marshall, Jr. and his co-workers, in Baltimore. The demonstration of this capacity is as yet limited largely to the excretion of most of certain foreign substances, such as phenol red, indigo-carmin, and hippuran. Marshall showed, in dogs, that when small doses of phenol red are injected subcutaneously, only 5 to 10 per cent of the dye is excreted by the glomeruli; the rest is excreted by the tubules. Homer W. Smith showed that the same is true concerning man. Richards and his associates demonstrated that indigo-carmin and hippuran are also excreted, for the most part, by the uriniferous tubules. It has not been shown that substances which are normal products of metabolism or constituents of the normal diet are excreted by the tubules.

From the uriniferous tubules the urine passes through the straight collecting tubules and papillary ducts into the calyces of the renal pelvis. Its transportation from the pelvis to the bladder is the function of the ureter.

BIBLIOGRAPHY

- ALBARRAN, JOAQUIN: *Exploration des fonctions des reins: étude medicochirurgical*. Paris: Masson et Cie, 1905.
- AMOLSCH, A. L.: Bilateral metanephric agenesis; report of 4 cases. *J. Urol.*, 38: 360, 1937.

- ANSON, B. J., *et al.*: Variations in the number and arrangement of the renal vessels. *J. Urol.*, 36: 211, 1936.
- ARDEN, FELIX: The history of renal physiology. *Med. J. Australia*, 25 (2): 335, August 27, 1938.
- AREY, L. B.: *Developmental Anatomy*. Phila., W. B. Saunders Co., Ed. 3, 1934.
- ASTRALDI, A.: Hypoplasie rénale congénitale. *Arch. urol. de clin. de Necker*, 7: 47, 1931.
- BAGEN, B.: Ein fall von doppelniere mit diagnostischen interesse. *Acta chir. Scandinav.*, 81: 36, 1938.
- BARDHAM, ERIK: Congenital kidney malformations and oligohydramnios. *Acta obst. et Gynec. Scand.*, 10: 134, 1930.
- BATES, G. S.: Bilateral renal agenesis in the fetus, associated with oligohydramnios. *Am. J. Obst. & Gynec.*, 25: 41, 1933.
- DAYLISS, L. E., *et al.*: The excretion of protein by the mammalian kidney. *J. Physiol.*, 77: 386, 1933.
- BEER, E., *et al.*: Heminephrectomy in disease of double kidney; 14 cases. *Ann. Surg.*, 108: 705, October 1938.
- BEER, E., AND FERBER, W. L. F.: Crossed renal ectopia (unilateral fused or elongated kidney). *J. Urol.*, 38: 541, 1937.
- BERGLUND, H., AND FRISK, A. R.: Uric acid elimination in man. *Acta med. Scandinav.*, 86: 233, 1935.
- BETHEA, J. A., AND PETERSON, W. L.: Unilateral fused kidney. *Am. J. Surg.*, 28: 368, 1935.
- BLUMGART, H. L., *et al.*: The action of diuretics in normal persons. *Arch. Int. Med.*, 54: 40, 1934.
- BOWMAN, W.: On the structure and use of the malpighian bodies of the kidney, with observations on the circulation through that gland. London, 1842.
- BOYD, A. M.: Anatomy and physiology of the kidney and ureter. *St. Bartholomew's Hosp. Repts.*, 68: 5, 1935.
- BOYD, EDITH: A method of establishing the probable rates of normal variation in the weights of organs. *Anat. Record*, 62: 1, 1935.
- BOYDEN, E. A.: Horseshoe kidney associated with left inferior vena cava and disc-shaped suprarenal glands, with note on the occurrence of horseshoe kidney in human embryos. *Anat. Rec.*, 51: 187, 1931.
- BRAASCH, W. F.: The clinical diagnosis of congenital anomaly in the kidney and ureter. *Ann. Surg.*, 56: 726, 1912.
- BRAASCH, W. F., AND HAMER, H. J.: Renal fusion: urographic data and their clinical significance. *British J. Urol.*, 10: 219, September 1938.
- BRAASCH, W. F., AND MERRICK, J. W.: Clinical and radiological data associated with congenital single kidney. *Surg. Gynec. & Obst.*, 67: 281, September 1938.
- BREMER, J. L.: The origin of the renal artery in mammals, and its anomalies. *Am. J. Anat.*, 18: 179, 1915.
- BROEDEL, MAX: The intrinsic blood vessels of the kidney and their significance in nephrectomy. *Bull. Johns Hopkins Hosp.*, 12: 10, 1901.
- BROMAN, I.: Ueber die entwicklung und bedeutung der mesenterien, etc. *Ergebn d. Anat. u. Entwicklungsgesch.*, 15: 332, 1906.
- BUGBEE, H. G., AND LOSEE, J. R.: The clinical significance of congenital anomalies of the kidney, etc. *Surg. Gynec. & Obst.*, 28: 97, 1919.
- CARLETON, A.: Crossed renal ectopia and its possible causes. *J. Anat.*, 71: 292, 1937.
- CARSON, W. J.: Supernumerary kidney. *Ann. Surg.*, 99: 796, 1934.
- CAMERON, G., AND CHAMBERS, R.: Direct evidence of function of the kidney in an early human fetus. *Am. J. Physiol.*, 123: 482, 1938.

- CAMPBELL, M. F.: Congenital absence of one kidney: unilateral renal agenesis. *Ann. Surg.*, 88: 1039, 1928.
- CHASIS, H., *et al*: Control of blood flow and glomerular filtration in normal man. *J. Clin. Investigation*, 17: 683, September 1938.
- COEN, E.: Descrizione anatomica di un feto senza reni e senza utero con altra anomalie. *Ann. Univ. di med. e chir.*, 267: 52, 1884.
- COLLINS, D. C. Congenital unilateral renal agenesis. *Proc. Staff Meet., Mayo Clin.*, 6: 581, 1931.
- CONWAY, E. J.: Structural laws of the mammalian kidney, with theoretical derivation. *Nature*, 139: 250, 1937.
- CUBITT, A. W.: The problem of anuria: a review of recent work on renal physiology. *British J. Surg.*, 24: 215, 1936.
- CUSHNY, A. R.: The excretion of urea and sugar by the kidney. *J. Physiol.*, 51: 36, 1917.
- CUSINY, A. R.: The secretion of the urine. N. Y., Longmans, Green & Co., 1917.
- DE VRIES, J. K.: Hypernephroma, papilloma and stone occurring in horseshoe kidney. *Am. J. Surg.*, 10: 487, 1930.
- DOMINGUEZ, R.: On the renal excretion of urea. *Am. J. Physiol.*, 112: 529, 1935.
- DORLAND, W. A. N.: A consideration of renal anomalies. *Surg. Gynec. & Obst.*, 1: 303, 1911.
- DRURY, D. R.: The physiology of the kidney from a clinical standpoint. *J. Urol.*, 41: 111, February 1939.
- EDWARDS, J. G.: The renal tubule and glomerulus. *Am. J. Physiol.*, 95: 493, 1930.
- EISENDRATH, D. N.: The relation of variations in the renal vessels to pyelotomy and nephrectomy. *Ann. Surg.*, 71: 726, 1920.
- EISENDRATH, D. N.: Congenital solitary kidney. *Ann. Surg.*, 79: 2206, 1924.
- EISENDRATH, D. N.: Hydroureter due to the obstruction of the renal pelvis by one of the two main renal arteries. *J. Urol.*, 24: 173, 1930.
- EISENDRATH, D. N.: Clinical importance of congenital renal hypoplasia. *J. Urol.*, 33: 331, 1935.
- ELLIS, Q. J.: A case of unilateral fused kidney (crossed ectopia). *Med. J. Australia*, 2: 561, October 1, 1938.
- ELSON, K. A., BOTT, P. A., AND WALKER, A. M.: The simultaneous measurement of renal blood flow and the excretion of hippuran and phenol red by the kidney. *Am. J. Physiol.*, 118: 739, 1937.
- EVANS, W. A., JR., AND GIBSON, J. G.: The blood volume in diuresis. *Am. J. Physiol.*, 118: 251, 1937.
- FELIX, W.: Development of the urinogenital organs. *Keibel-Mall: Manual of Human Embryology*, Vol. II, Chapt. 9. Phila., J. B. Lippincott Co., 1912.
- FOOTE, J. J., AND GRAFFLIN, A. L.: Quantitative measurements of fat-laden and fat-free segments of proximal tubules in nephron of the cat and the dog. *Anat. Rec.*, 72: 169, October 25, 1938.
- GAGE, S. P.: A three weeks human embryo, with special reference to the brain and nephric system. *Am. J. Anat.*, 4: 409, 1905.
- GEISINGER, J. F.: The recuperative power of the kidney: report of 3 cases. *J. Urol.*, 37: 639, 1937.
- GEISINGER, J. F.: Supernumerary kidney. *J. Urol.*, 38: 331, 1938.
- GOLDSTEIN, A. E.: Anatomy and physiology of the kidney. *Lewis's Practice of Surgery*, VIII, Chapter III, p. 1.
- GOLDSTEIN, A. E.: Congenital absence of one kidney: review of literature and report of 2 cases. *Southern M. J.*, 18: 750, 1925.

- GOLDSTEIN, A. E., AND SHAW, C. C.: Bilateral supernumerary fused kidney, with reduplication of ureters, etc. *Urol. & Cutan. Rev.*, 41: 459, 1937.
- GOWAR, F. J. S.: Anephrogenesis. *J. Obst. & Gynec. British Emp.*, 42: 871, 1935.
- GUIZZETTI AND PARISETS: quoted by Gunther.
- GRUBER, C. M.: The autonomic innervation of the genito-urinary system. *Physiological Rev.*, 13: 497, 1933.
- GUNTHER, HANS: Die sexualdisposition bei erkrankungen der harnorgane. *Ztschr. f. Urol.*, 23: 778, 1929.
- GUTIERREZ, ROBERT: The clinical management of the horseshoe kidney. N. Y., P. B. Hoeber, 1934. Also: *Am. J. Surg.*, 14: 657, 1931.
- GUTIERREZ, ROBERT: Surgical aspects of renal agenesis, etc. *Arch. Surg.*, 27: 686, 1933.
- GUTIERREZ, ROBERT: Role of anomalies of kidney and ureter in causation of surgical conditions. *J. A. M. A.*, 106: 183, 1936.
- HAIN, A. M., AND ROBERTSON, E. M.: Coogenital urogenital anomalies of rats including unilateral renal agenesis. Further data in support of their inheritance. *J. Anat.*, 372: 83, 1937.
- HARRIS, A.: Congenital solitary kidney, etc. *Urol. & Cutan. Rev.*, 41: 613, 1937.
- HAWES, G. A.: Renal hypoplasia. case report. *J. Urol.*, 42: 500, 1939.
- HAYMAN, J. M., JR., AND MARTIN, J. W., JR.: Anatomic and physiologic basis of renal function tests. *Trans. Assoc. Am. Physicians*, 52: 182, 1937.
- HEIDENHAIN, R.: Versuche über den Vorgang der Harnabsonderung. *Arch. f. d. Ges. Physiol.*, 9: 1, 1874.
- HERBST, R. H., AND APPELBACH, C. W.: Hypoplasia of the Kidney. *Surg. Gynec. & Obst.*, 61: 306, 1935.
- HERMAN, J. L., AND FETTEROLF, G.: Dumb-bell kidney. *Ann. Surg.*, 57: 868, 1913.
- HERMAN, LEON: Renal anomaly. *Surg. Clin. N. Am.*, 4: 265, 1934.
- HILL, E. C.: On the first appearance of the renal artery and the relative development of the kidneys, etc. *Johns Hopkins Hosp. Bull.*, 16: No. 167, 1905.
- HINMAN, F., MORISON, D. M., AND LEE-BROWN, R. K.: Methods of demonstrating the circulation in general, as applied to a study of the renal circulation in particular. *J. A. M. A.*, 81: 177, 1923.
- HUNDLEY, J. M., JR., *et al*: Physiologic and pathologic observations on the urinary tract during pregnancy. *Surg. Gynec. & Obst.*, 66: 36, Feb. (No. 2A) 1938.
- HUNTINGTON, G. S., AND McCLURE, C. F. W.: The development... of the postcava and axillary veins... in the adult. *Anat. Rec.*, 20: 1, 1920.
- HYMAN, A.: Renal hypoplasia and aplastic kidney. *J. Mt. Sinai Hosp.*, 4: 253, 1937.
- JARMAN, W. D.: Surgery of horseshoe kidney with post-aortic isthmus. *J. Urol.*, 41: 1, July 1938.
- JASIENSKI, G.: Les lymphatiques du rein sain. *J. d'Urol.*, 40: 97, 1935.
- JEDELL, H.: A note on the source and character of the blood vessels in the kidney. *Anat. Rec.*, 5: 47, 1911.
- JONA, J. L.: Graphic studies of the contractions of the kidney pelvis. *Surg. Gynec. & Obst.*, 56: 628, 1933.
- JONA, J. L.: The kidney pelvis: a further contribution to its physiology and pathology. *Surg. Gynec. & Obst.*, 59: 713, 1934.
- JORDAN, H. E., AND KINDRED, J. L.: A Textbook of Embryology. N. Y., D. Appleton & Co., 1926.
- JUDD, E. S., AND HARRINGTON, S. W.: Ectopic or pelvic kidney. *Surg. Gynec. & Obst.*, 28: 446, 1919.
- KATZ, L. N., *et al*: Factors concerned in renal hypertension. *Proc. Soc. Exper. Biol. & Med.*, 37: 722, January 1938.

- KEMPTON, R. T.: Nussbaum's experiment in renal secretion. *Am. J. Physiol.*, 119: 175, 1937.
- KIMBROUGH, J. C.: Hypoplasia of the kidney. *Urol. & Cutan. Rev.*, 41: 702, 1937.
- KINT, M. G., AND KESAVASWAMI, P.: Case of hydronephrosis in congenital fused kidney. *Brit. J. Urol.*, 10: 266, September 1938.
- KRETSCHMER, H. L.: Supernumerary kidney. *Surg. Gynec. & Obst.*, 48: 818, 1929.
- LASSEN, H. C. A., AND HUSFELDT, E.: Kidney function and blood pressure. *J. Clin. Investigation*, 12: 263, 1934.
- LEE-BROWN, R. K.: The renal circulation. *Arch. Surg.*, 8: 831, 1924.
- LEE-BROWN, R. K., AND LAIDLEY, J. W. S.: Some observations on microscopical anatomy of the kidney. *J. Urol.*, 21: 259, 1929.
- LEGUEU, F.: Hypoplasie rénale, discussion. *Bull. Soc. franc. d'urol.*, p. 62, February 17, 1930.
- LOWSLEY, O. S.: Modern renal surgery—with particular reference to heminephrectomy. *N. Y. State J. Med.*, 36: 591, 1936.
- LOWSLEY, O. S.: Anomalies of the kidney and movable kidney. *Lewis's Practice of Surgery*, Vol. VIII, Chpt. IV. Hagerstown, Md., W. F. Prior Co., Inc., 1935.
- LUDWIG, C.: Nieren und Harnbereitung. In *Wagner's Handb. d. Physiol.*, 2: 628, 1844.
- MACKENZIE, D. W., AND HAWTHORNE, A. B.: Unilateral renal aplasia. *Surg. Gynec. & Obst.*, 46: 42, 1928.
- MACKENZIE, D. W., AND HAWTHORNE, A. B.: Ectopic kidney. *Trans. Am. Assoc. Genito-Urin. Surg.*, 30: 121, 1937.
- MARION, G.: Hypoplasie rénale, discussion. *Bull. Soc. franc. d'urol.*, p. 50, March 17, 1930.
- MARSHALL, E. K., JR.: The secretion of phenol red by the mammalian kidney. *Am. J. Physiol.*, 99: 77, 1931.
- MARSHALL, E. K., JR.: The comparative physiology of the kidney in relation to theories of renal secretion. *Physiol. Rev.*, 14: 133, 1934.
- MARSHALL, E. K., JR., AND CRANE, M. M.: The secretory function of the renal tubules. *Am. J. Physiol.*, 70: 465, 1924.
- MARSHALL, E. K., JR., AND GRAFFLEN, A. L.: The function of the proximal convoluted segment of the renal tubule. *J. Cell. & Comp. Physiol.*, 1: 161, 1932.
- MAYERS, M. M.: Crossed ectopia of the kidneys. *J. Urol.*, 36: 3, 1936.
- MCCLURE, C. F. W., AND BUTLER, E. G.: The development of the vena cava inferior in man. *Am. J. Anat.*, 35: 331, 1925.
- MILLIKEN, J. F., AND KARR, W. G.: The influence of the nerves on the kidney function in relation to the problem of kidney function. *J. Urol.*, 13: 1, 1925.
- MOORE, T. D.: Congenital solitary hydronephrotic kidney; pyelo-ureteroplasty. *J. Urol.*, 27: 581, 1932.
- MORISON, D. M.: A study of the renal circulation, with special reference to its finer distribution. *Am. J. Anat.*, 37: 53, 1926.
- NEEDHAM, JOSEPH: Chemical embryology. Cambridge Univ. Press, 1931.
- NEEDHAM, JOSEPH: The history of embryology. Cambridge Univ. Press, 1934.
- NICHOLSON, G. W.: The kidneys and development. *Guys, Hosp. Repts.*, 77: 362, 1927.
- NICOLESKO, I.: Vaisseaux et ganglions lymphatiques du bassin. *Ann. d'anat. path.*, 6: 1251, 1929.
- NICOLESKO, I.: Un nouveau colorant pour les recherches de lymphatiques. *Ann. d'anat. path.*, 7: 150, 1930.
- OCKERBLAD, N. F., et al.: Hypernephroma in a double kidney. *Brit. J. Urol.*, 10: 259, September 1938. Also: *J. Urol.*, 40: 572, November 1938.
- PAPIN, E.: Anomalies congénitales du rein. *Encyclopedie franc. d'urol.*, 11f; 227, Paris, Doin et fils, 1914.
- PAPIN, E., AND LEISENRATH, D. N.: Les anomalies des reins et des urètres. *Arch. d. mal. d. reins*, 2: 421, 1926.

- PAPIN, E., BERNASCONI, ET BERNARD: Contribution à l'étude du rein surnuméraire. *Arch. d. mal. d. reins*, 6: 1, 1931.
- PARKER, ALICE E.: Studies on the main posterior lymph channels of the abdomen and their connection with the lymphatics of the genito-urinary system. *Am. J. Anat.*, 56: 409, 1935.
- PATCH, F. S.: Crossed heterolateral ectopic kidney without fusion. *Brit. J. Urol.*, 9: 339, 1937.
- PEARLMAN, S. J.: Bilateral supernumerary fused kidneys, etc. *Urol. & Cutan. Rev.*, 41: 479, 1937.
- PEDROSO, G.: "Rein en galette" or shield-shaped kidney. *J. Urol.*, 24: 389, 1930.
- PEMBREY, M. S.: The process of excretion in the kidney. *Guy's Hosp. Repts.*, 77: 373, 1927.
- PENA, A. DE LA, AND PENA, E. DE LA: Hydronephrosis gauche... d'une hypoplasie congénitale. *J. d'urolog.*, 44: 335, 1937.
- POHLMAN, A. G.: A note on the development relations of the kidney and ureter in human embryos. *Johns Hopkins Hosp. Bull.*, 16: No. 167, 1905.
- POHLMAN, A. G.: Abnormalities in the form of the kidney and ureter dependent upon the development of the renal bud. *Johns Hopkins Hosp. Bull.*, 16: 197, 1914.
- PRICE, D. E.: Anephrogenesis. *Lancet*, 1: 997, April 30, 1938.
- RASO, MARIO: Assenza congenita bilaterale del rene. *Pathologica*, 29: 459, 1937.
- REHBERG, P. B.: Studies on kidney function. *Biochem. J.*, 20: 447, and 461, 1926.
- RICHARDS, A. N.: Methods and results of direct investigation of the functions of the kidney. *Beaumont Found. Lect.*, Ser No 8. Baltimore, Williams & Wilkins Co., 1929.
- RICHARDS, A. N.: Physiology of the kidney. *Penn. Med. J.*, 33: 527, 1930.
- RICHARDS, A. N.: Physiology of the kidney. *Bull. N. Y. Acad. Med.*, 14: 5, January 1938.
- RICHARDS, A. N. AND WALKER, A. M.: Quantitative studies of the glomerular elimination of phenol red and indigo carmine in dogs. *J. Biol. Chem.*, 87: 479, 1930.
- RICHARDS, A. N., WESTFALL, B. B., AND BOTT, P. A.: Insulin and creatinine clearance in dogs, etc. *J. Biol. Chem.*, 116: 749, 1936.
- ROLNICK, H. C.: Some observations on the renal capsule. *J. Urol.*, 38: 421, 1937.
- ROSENBAUM, R.: Ueber doppelseitige Nierenaplasie. *Frankfurt Ztschr. f. Path.*, 41: 136, 1931.
- ROSS, J. C.: Decapsulation and denervation of the kidney. *Liverpool Med.-Chir. J.*, 46 (Pt. I): 78, 1938.
- RUMPEL, O.: Nierenreaktion bei einseitiger Langniere (gekreuzte Dystopie). *Zentralb. f. Chir.*, 59: 1290, 1932.
- SACCONE, A. AND HENDLER, H. B.: Supernumerary kidney: report of case and review of the literature. *J. Urol.*, 31: 311, 1934.
- SCHACKELFORD, R. T.: Left urogenital maldevelopment. *Am. J. Surg.*, 35: 117, 1937.
- SCHUMACKER, H. B., JR.: Congenital anomalies associated with unilateral renal agenesis. *Arch. Surg.*, 37: 596, October 1938.
- SMITH, H. W.: The physiology of the kidney. N. Y., Oxford Univ. Press, 1937.
- SSYSGANOW, A. N.: Ueber das Lymphsystem der Nieren und Nierenhüllen beim Menschen. *Ztschr. f. d. ges. Anat. (Abt. 1)*, 91: 771, 1930.
- STERLING, W. C., AND LANDS, A. M.: An experimental study of injuries to the kidney. *J. Urol.*, 37: 466, 1937.
- STEVENS, A. R.: Single pelvic kidneys. *J. Urol.*, 37: 610, 1937.
- STEVENS, W. L.: Kidney anomalies; report of a case of bilateral fusion of a supernumerary kidney. *Calif. & West. M. J.*, 23: 294, 1925.
- STEVENS, W. E.: Observations on female urology, with special reference to ectopic kidneys. *J. Urol.*, 35: 241, 1936.

- STEWART, A. B.: Congenital absence of one kidney. *Brit. J. Urol.*, 5: 147, 1933.
- THEOBALD, G. W., AND VERNEY, E. B.: *The inhibition of water diuresis by afferent nerve stimuli after complete denervation of the kidney.* *J. Physiol.*, 83: 341, 1935.
- THOMAS, G. J., AND BARTON, J. C.: Ectopic pelvic kidneys. *J. A. M. A.*, 106: 197, 1936.
- THOMPSON, G. J., AND ALLEN, R. B.: Unilateral fused kidney. *Surg. Clin. North Am.*, 14: 729, 1934.
- THOMPSON, G. J., AND PACE, J. M.: Ectopic kidney; review of 97 cases. *Surg., Gynec. & Obst.*, 64: 935, 1937.
- TRAINOR, D. C.: Congenital solitary kidney: 3 cases. *Med. J. Australia*, 2: 352, 1937.
- TRAUT, H. F.: The structural unit of the human kidney. *Contrib. Embryol. (Carnegie Inst., Wash.)* 15: 103, 1923.
- UBELHOR, R.: Beitrag zur klinik der hypoplasia renis. *Ztschr. f. Urol.*, 27: 79, 1933.
- VERLIAC, PAFIN, E., AND ASTRALDI, A.: L'hypoplasie rénale. *Bull. Soc. franc. d'urol.*, No. 2, p. 56, Feb. 17, 1930.
- WALD, H.: Weight of the normal adult human kidney and its variability. *Arch. Pathol.*, 23: 493, 1937.
- WILMER, H. A.: Unilateral fused kidney; report of 5 cases and review of literature. *J. Urol.*, 30: 551, 1938.
- WINTON, F. R.: *The glomerular pressure in the isolated mammalian kidney.* *J. Physiol.*, 72: 361, 1931.
- WINTON, F. R.: *The control of the glomerular pressure by vascular changes within the kidney.* *J. Physiol.*, 73: 151, 1931.
- WINTON, F. R.: *The influence of venous pressure on the isolated mammalian kidney.* *J. Physiol.*, 72: 49, 1931.
- WINTON, F. R.: Physical factors involved in activities of the mammalian kidney. *Physiol. Rev.*, 17: 408, 1937.

CHAPTER XXXVII

INJURIES AND DISEASES OF THE KIDNEY

A. INJURIES OF THE KIDNEY AND RENAL PELVIS

Injuries of the Kidney

Although the kidney is fairly well protected from trauma by reason of its mobility and position, injuries to it have increased considerably during recent years, mainly as a result of the increasing frequency of automobile and industrial accidents. Athletic sports also contribute their share of renal injuries.

Etiology. Injury to the kidney may occur as the result of (1) *direct trauma*—kicks or blows in the loin or back, falls upon hard surfaces or objects, crushing accidents, or any cause which brings force to bear directly over the kidney area; (2) *indirect trauma*—transmitted violence from falls from heights onto the feet or buttocks; (3) *violent muscular effort*, such as the lifting of heavy objects, or sudden movements made in dodging blows or reaching to catch something; (4) *gunshot or stab wounds*. Rupture due to direct violence is by far the most common form of injury seen in civil practice.

Renal rupture secondary to some pathological condition, with or without trauma (spontaneous rupture), is rare. Most cases of spontaneous rupture occur in hydronephrosis, but rupture in tuberculosis, abscess, calculus, and tumor has been reported.

An apparently trivial accident may cause severe injury to the kidney. Sometimes a considerable interval may elapse before hematuria or other evidences of trauma are noted by the patient, and, if the accident has been slight, he may then have difficulty in recalling how or when he was injured. The kidneys are so well protected anatomically, however, that as a rule considerable force or pressure is required to injure them.

The mechanics involved in rupture of the kidney from direct or indirect trauma were studied experimentally by Kuester (1896), who found that when the kidney is subject to direct trauma, or is forced, by transmitted violence, against the twelfth rib or upper lumbar transverse process, it behaves like a ball of fluid, transmitting the impact in all directions.

The resistance offered by the kidney to external violence appears to

be largely determined by the strength of its fibrous capsule. In experiments conducted by Lowsley, it was found impossible to rupture the fibrous capsule of a dog's kidney by striking upon its surface with a blunt instrument, although various degrees of injury could be inflicted on the cortex, depending upon the amount of force exerted. The injuries varied from slight subcapsular hemorrhage to complete pulpefaction of the traumatized section. Upon opening the fibrous capsule following the injury, brisk bleeding always occurred, and, in the case of severe injury, serious hemorrhage was noted. The fibrous capsule may, however, be digested by the ferments released by traumatism to the cortical substance, resulting in perinephritis, infiltration with urine and pus, and, in many cases, complete destruction of the kidney and menace to the life of the patient.

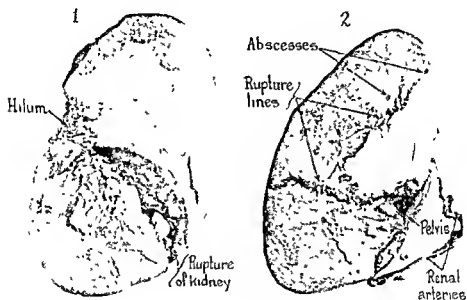
When Stirling and Lands undertook similar experimentation, they applied force to a considerable area of kidney surface, which, they reported, produced such tension of the fibrous capsule as to cause it to rupture. They believed that a blow applied to a relatively small area might produce considerable damage to the parenchyma under the place where the blow fell, without causing any great increase in capsular tension; but they felt that the type of blow employed by them was more nearly comparable to those most likely to fall upon human kidneys—in automobile accidents and similar catastrophes—than the type of trauma employed in our experiments.

Pathology. *Contusions and Ruptures.* Injury to the kidney may vary all the way from tears of the fatty capsule without injury to the kidney, localized subcapsular hemorrhage, slight contusion of the parenchyma, a single small fissure in the parenchyma, or other comparatively trivial lesions, to rupture of the renal pelvis, rupture of the parenchyma, capsule, and pelvis, complete severance of the kidney into two or more pieces, rupture of the vascular pedicle and tearing off of the ureter, or general pulpefaction—with or without complicating rupture of the peritoneum or injury to adjacent structures.

Rupture of the kidney with tearing of the fibrous capsule is usually more serious than rupture of the parenchyma alone. When the capsule is intact, the hemorrhage remains under the capsule in the form of an ecchymosis or hematoma. In extensive pulpefaction, the hemorrhage may be rapidly fatal. If the capsule is also torn, there will be more or less extensive extravasation of blood into the perirenal tissues. Small extravasations may be readily and completely absorbed; in more ex-

tensive cases large perirenal hematomas form, which may in time become encysted and their walls thickened and even calcified. If a calyx or the pelvis is lacerated, there will be extravasation of urine into the perirenal tissues. When the peritoneum is uninjured, urine or blood, or both, after distending the perirenal space, may extend down through the inguinal and femoral canals to the scrotum and thigh.

The chief complications of renal injury are hemorrhage and infection. Hemorrhage is the most constant and immediate danger. The bleeding varies with the type and degree of injury, but is present in all cases, al-



though blood does not always appear in the urine. If the vascular pedicle is torn, the hemorrhage is usually so great as to cause prompt death from exsanguination. In less severe blood losses, where the patient survives, the kidney will become necrotic and, if the capsule has been torn, be surrounded by a large clot.

A second and only slightly more remote danger is infection, which plays a very important part in renal trauma. The pathological picture may be altered at any moment by the intervention of bacterial agents. An infected perirenal hematoma quickly turns to a perirenal abscess.

Nowhere do microorganisms grow better than in such a clot, and, if extravasation of urine also takes place, or if the trauma is of such a nature that it has actually carried infection in to the site of injury, the stage will be set for the playing of a most virulent role by whatever infectious agent has gained entrance. Infection may be carried in by a ureteral catheter, introduced to a pelvis which has been lacerated and filled with blood that is partly coagulated but sterile, or it may be carried to such a pelvis by a blood stream infection from another source. There are so many ways for microorganisms to reach an injured kidney that the sequel of infection is almost inevitable.

If the infection is mild, the injurious results will be merely denser fibrosis and more extensive cicatricial distortion with healing. The more serious cases eventuate in pyonephrosis, with more or less complete destruction of the kidney, even if the traumatic injury was originally slight.

Gunshot and Stab Wounds. Gunshot and other puncture wounds of the kidney are fairly frequent in war-time but uncommon in civil life. Such wounds are inflicted by bullets, shrapnel, fragments of shell, bayonets, stilettos, slivers of glass or metal, or spicules of bone. The seriousness of the wound varies with the extent of damage to the large blood vessels, the degree of infection, and the injuries to neighboring structures.

Shell wounds, which are usually large and destructive, and almost always associated with grave injuries to other abdominal viscera, as a rule require primary nephrectomy.

Bullet wounds involving the hilum usually sever the vascular pedicle—demanding immediate surgical intervention. The passage of a bullet through any part of the kidney as a rule causes considerable destruction of the parenchyma, particularly if the weapon from which the bullet came is a high-powered rifle. If the injury is close to one pole, this entire area may be torn away, and there is usually considerable hemorrhage into the parenchyma beyond the damaged area. Sometimes the kidney may be completely split in two. In all cases in which there is much destruction of renal tissue from the entrance of the missile, the fibrous, as well as the fatty capsule, will be badly torn. If the injury is in the renal pelvis, there will be extravasation of urine into the surrounding tissues, and there is likelihood of some of the larger vessels participating in the trauma, resulting in profuse and oftentimes rapidly fatal hemorrhage. When the peritoneum is injured, the extravasated urine will, in

all probability, set up a generalized peritonitis, and, even if the peritoneum escapes unscathed, a subphrenic abscess may result from the urinary extravasation.

As a rule, other abdominal viscera will be injured, especially the stomach, duodenum, and colon.

Rupture of Previously Diseased Kidney: Importance in Industrial Surgery. *Traumatic Rupture.* A previously diseased kidney is much more liable to traumatic injury than a sound one, and the outcome will, of course, be greatly influenced by pre-existing pathological conditions. This is of especial importance in damage suits and industrial surgery, for most cases of renal trauma are the result of automobile accidents or involve injuries suffered by workers in the pursuit of their occupations. The necessity for fixing liability, which has arisen since the enactment of workmen's compensation laws, has rendered increasingly important the determination of the exact mechanism by which such accidents as kidney rupture occur, and whether the lesion is wholly due to the trauma sustained or is influenced by pre-existing conditions.

When undoubted injury has been sustained by the kidney, it still remains at times a difficult matter to decide whether the urinary symptoms existed before the accident but were thereupon aggravated, or whether a perfectly honest patient may not have first noticed pre-existing symptoms after the accident had called his attention to them. The problem of deciding how great a factor in the present disability the trauma really has been may be a very difficult one.

Spontaneous Rupture (Non-Traumatic). A diseased kidney may also rupture without trauma (spontaneous rupture). While this is rare, it has been reported often enough to make its consideration necessary in cases where there is doubt as to the responsibility of an employer.

In 1924, Henline reported from our service a case of spontaneous rupture of the kidney and cited 24 others—all that he was able to collect from the literature. In 1932, Mathé added 4 cases personally seen by him.

Some form of renal disease which weakens the walls of the kidney or renal pelvis is a prerequisite to spontaneous rupture. Hydronephrosis or lithiasis is the etiological factor in most instances; but there have been reported causes as widely varying as tuberculosis, abscess, tumor, necrosis of the suprarenal gland, and renal arteriosclerosis—with chronic nephritis always present. When the wall has been weakened by disease, back pressure due to ureteral obstruction or reflux from the bladder may exert

enough extra pressure to rupture the kidney. It is well for one doing retrograde pyelography to bear in mind the possibility of rupture when the pelvis or kidney parenchyma is known to be weakened by previous disease.

Any moderate exertion may cause rupture of such a diseased kidney—hence the importance of establishing the previous existence of the conditions predisposing to rupture.

The pathological findings in spontaneous rupture of the kidney, while in general resembling those of traumatic rupture, will be complicated and modified by the pre-existing disease.

The chief symptoms are sudden, severe pain in the kidney region, symptoms of internal hemorrhage, and the presence of a retroperitoneal tumor. Death usually results in a short while from anemia, infection, or uremia due to the chronic nephritis. Surgery is the only hope, and usually consists of nephrectomy—although, if the capsule is intact and there is no infection, drainage may suffice. Rarely, spontaneous rupture may occur without these symptoms, but may manifest itself by an insidious onset and the development of a perinephritic abscess. In the case reported by Henline, the spontaneous rupture of the kidney resulted in a perinephritic abscess which burrowed its way through the body wall and presented itself as an extravasation of urine in the suprapubic region, scrotum, and perineum.

Symptoms of Renal Injury. Though textbooks for many years have listed a number of "classical" symptoms of renal injury, it has been our experience that the symptoms seldom conform to the accepted rules, and, in the words of a recent writer, "may be a poor index to the gross kidney injury." In many cases of kidney trauma there will be associated injuries to other viscera, fracture of the pelvis, or injuries to the spine, so that the renal injury is frequently overlooked at the time or its importance greatly minimized.

The chief symptoms are shock, hematuria, pain, a mass in the loin, and rigidity of the affected side. Shock varies with the severity of the injury and the extent of hemorrhage. If there is much hemorrhage, its effect upon the pulse rate, blood pressure, and the general clinical picture will immediately be apparent. Pain is always present. The pain may be generalized over the abdomen, or may radiate to the back, shoulder, hip, sacrum, or the lumbar region. The passage of blood clots causes pain resembling renal colic due to calculus.

Hematuria is present in a high percentage of cases, but unless the pa-

tient's condition permits cystoscopic or urographic investigation, it may be impossible to establish definitely that the blood is coming from the kidney. If the hematuria increases—more blood appearing in the urine at each voiding—the suspicion of kidney trauma is greatly increased. If the ureter has escaped injury, the patient can often void without difficulty, but the bladder contents may be practically pure blood.

Although hematuria is a common and important sign, the absence of blood in the urine does not rule out injury to the kidney; nor can the extent of the renal damage be estimated by the amount of blood in the urine. If there is no hematuria, it may be due to severance of the ureter, complete blockage of the ureter by a blood clot, or to reflex anuria following injury to the kidney. If the peritoneum is torn, the blood escapes into the peritoneal cavity. Very frequently there is extravasation of blood into the perirenal tissues—another factor which makes observations upon the amount of blood in the urine of uncertain diagnostic value. If the patient seems but slightly shocked at first, but later relapses into profound shock, the occurrence of profuse hemorrhage is almost a certainty.

Moving a patient with a ruptured kidney may cause additional bleeding by disturbing the clots which have formed at the site of the injury.

Spontaneous rupture of the kidney, as previously noted, is usually manifested by sudden, sharp pain in the renal area, symptoms of internal hemorrhage, and the development of a retroperitoneal tumor. If the right kidney is the one affected, the presence of localized rigidity, local or diffuse tenderness, and generalized abdominal pain may suggest a ruptured appendiceal abscess. If the hemorrhage is profuse (as it usually is), there will be the usual symptoms of profound shock, with immediate subnormal temperature followed by a characteristic elevation due to the absorption of fibrin ferment (Doll).

Diagnosis. A history of trauma, hematuria, and pain is strongly suggestive, though not conclusive. External evidence of injury may be absent. Bimanual palpation is valuable in localizing the injury, and will usually reveal more or less swelling in the loin, as well as rigidity and localized or diffuse tenderness.

A hemoglobin percentage and total red-cell count is of the greatest importance.

Cystoscopy and pyelography give invaluable information, not only as to the injured kidney but also regarding the function of the other side. Very often, however, the condition of the patient will not permit such

investigation, and, in every case, there is danger of introducing infection into the lacerated tissues. Excretion urography is superior to any other method at our disposal in these cases. Intravenous injections of opaque solution can be given even to an unconscious patient, and this method should prove of great help in many cases. Urography will show a normal kidney on one side if the injury is unilateral, and some function on the injured side. Extensive rupture communicating with the pelvis and calyces will be revealed by extravasation of the opaque solution into the subcapsular tissues and renal parenchyma. If the renal injury results in surrounding the kidney with a zone of edema and hemorrhage, the x-ray may reveal characteristic changes in the position and contour of the pelvis and ureter.

Plain x-rays are also very valuable in determining perirenal hemorrhage, and may be taken when a patient is too seriously injured for cystoscopic and pyelographic investigation. Suggestive, though not pathognomonic roentgenographic appearances are: obliteration of the psoas line; flexion of the spine toward the injured side; haziness or apparent enlargement of the kidney shadow; limitation or fixation of the kidney's mobility.

In cases where there is doubt as to the traumatic nature of the renal lesion, certain other conditions affecting the kidney must always be ruled out. These are perinephritic abscess, which may be impossible to recognize except upon exploration, and new growth, tuberculosis, and certain non-specific infections—all of which may give x-ray pictures closely simulating renal trauma.

Prognosis. In uncomplicated renal injuries of moderate degree the prognosis is good, and many patients will recover under expectant treatment. In more serious injuries, with severe hemorrhage, the prognosis depends on how promptly surgery is instituted. When the injuries are part of extensive trauma to the abdominal viscera, the mortality is very high.

The remote possibilities of kidney injury must be considered. The destruction of renal parenchyma may lead to permanent loss of function. Rupture of the parenchyma into the calyces or pelvis, or injury of the pelvis alone or of the upper portion of the ureter, is likely, in healing, to result in cicatricial distortion of a calyx or the pelvis, and this, by impeding normal drainage, will lead to hydronephrosis. Thus, cases which urography showed to be healing well may subsequently develop into grave chronic conditions due to permanent urinary-tract damage.

The necessity of following up every case of renal injury long after healing has ensued should therefore be emphasized.

Numerous cases are on record of calculi which apparently formed as a direct sequel to traumatic injury. The setting up of obstruction and retention provides conditions admirably suited to stone-formation. A blood clot or a fragment of necrosed tissue may form the nucleus about which urinary salts are rapidly deposited.

The remote possibility of cyst-formation has been emphasized by Colston and Baker, who, in considering the later sequelae of renal injuries, found that of 13 cases of such trauma, 6, or more than 40 per cent, had later cyst-formation, which would indicate that previous trauma may be responsible for the occurrence of renal cysts far more often than diagnosticians are aware.

Treatment. The treatment depends upon the severity of the injury, the general condition of the patient, and the coincidence of other injuries. As one peruses the late literature, the efforts to conserve traumatized kidneys become more noticeable and continuously more successful.

If there is no sign of extensive hemorrhage or shock, or if intravenous pyelography can be done and the pyelogram shows no extravasation from the kidney, pelvis, or ureter, expectant treatment is indicated, but the patient should be observed carefully as to blood pressure, pulse rate, and the appearance of the urine. Sedatives are usually required to relieve the pain, which even in slight traumatism is severe. Fluids in generous amount should be permitted but they should not be forced. Urinary antiseptics should always be administered, in an endeavor to prevent infection of the kidney and bladder.

If the shock is great, the patient should be given supportive treatment, including blood transfusion, and exploratory operation done at the earliest safe moment. If the injury has not been grave at the outset, but hematuria continues for longer than 24 hours, or if tenderness or swelling, or both, persist in the loin (even if there is no hematuria), exploratory operation should be done.

The treatment of traumatized kidneys is further discussed under Operative Treatment of Renal Injuries (p. 1695).

Injuries of the Renal Pelvis

Injury to the renal pelvis is uncommon. In severe crushing accidents the entire organ may be reduced to a pulp, the pelvis suffering with the rest of the renal tissue. In general, however, the pelvis is less often traumatized than the renal parenchyma.

Etiology. Most injuries to the renal pelvis can be grouped under three heads: (1) rupture from external force, (2) spontaneous rupture, (3) perforation by ureteral catheters, bougies, etc., or rupture by excessive pressure during injection of pyelographic media. The first two types have already been considered when discussing traumatic and spontaneous rupture of the entire renal organ.

External trauma is the most common causal factor. Spontaneous rupture usually supervenes upon long-standing hydronephrosis, where the pelvic wall has become so thinned out by *constant distention* that it finally gives way; or a stone may form within the pelvis, or be expelled into the pelvis from a calyx or from higher up, and, by erosion, gradually establish the conditions favoring rupture.

A few instances of rupture of the renal pelvis following plastic operation for stricture at the ureteropelvic junction have been recorded. The immediate cause is either a recurrence of the original obstruction, for relief of which the operation was performed, or the production of a new obstruction, which exerts back pressure of retained urine upon the suture line at the ureteropelvic junction.

Resection of the pelvis for hydronephrosis may lead to rupture if proper precautions are not taken at the time of operation.

Rupture of the kidney pelvis by excessive pressure during the injection of pyelographic solution has been reported numerous times. The extravasation may be limited to the parenchyma, or may extend through the capsule into the perirenal tissues. Such ruptures are much more likely to occur in the presence of chronic inflammation, ulceration, stone, marked hydronephrosis, or any lesion which has caused weakening of the walls of the kidney. They are also more apt to take place when the syringe method is used for injection. Shapiro and Veseen (1930) reported 5 deaths following bilateral pyelography, in 4 of which the syringe method was used. In kidneys whose walls have been weakened by disease, filling the pelvis to the point of discomfort is a dangerous procedure.

The renal pelvis, like the ureter, may be perforated by a ureteral catheter or bougie. Such accidents occur more frequently in infants and children. It is unlikely that a normal renal pelvis in an adult can be perforated by the ordinary ureteral catheter, but such perforation may occur when the catheter is reinforced with a wire stylet.

Pathology. Lacerations or perforations of the renal pelvis usually occur on its posterior surface, as would naturally be expected from the

anatomical arrangement and the approach afforded to instruments in particular. Any tear in the pelvis is likely to be radial, especially if a hydronephrotic pelvis has been traumatized by external force or has ruptured spontaneously. The laceration usually extends from a point near the junction of the pelvis and ureter in a direction corresponding to that taken by the uriniferous tubules. The extent of the rupture will, in general, bear some relation to the degree of back pressure of fluid, or intrapelvic pressure, which induced the rupture. The extrarenal type of pelvis is more susceptible to injury than the intrarenal.

When the kidney itself is the main site of injury, a tear in the parenchyma is likely to extend into the pelvis, if the latter is weakened by disease. Rupture of any of the calyces may also occur. When the calyceal rupture is due to trauma, the laceration may extend partly or completely through the adjacent parenchyma, which results in the extravasation of blood and urine below the true capsule of the kidney and heals with little or no permanent damage to the kidney.

Symptoms: Diagnosis: Treatment. The symptoms, diagnosis, prognosis, and treatment of traumatic injuries to the renal pelvis do not differ from those of injuries to the kidney proper.

B. DISEASES OF THE KIDNEY AND RENAL PELVIS

Hydronephrosis

Definition. "Hydronephrosis" is the term applied to dilatation of the renal pelvis and calyces with retained urine, and the pressure atrophy of the parenchyma resulting therefrom. The degree of dilatation varies in every case, and ranges from a slightly distended kidney, little larger than normal, to an enormous urine-distended sac occupying the greater part of the abdominal cavity.

Hydronephrosis with suppuration is termed *infected hydronephrosis*; this is to be distinguished from *pyonephrosis*, which is a closed suppurating kidney that follows an extensive pyelonephritis. In pyonephrosis, pelvic distention is absent or very slight, and is caused by pus and not by urine. An infected hydronephrosis may, however, progressively become a pyonephrosis.

Intermittent hydronephrosis occurs when the cause of the obstruction is movable or variable, *i.e.*, a calculus lodged in the ureter, which shifts from time to time, permitting urine to pass.

The first mention in medical literature of hydronephrosis as a clinical entity appears to have been in Rayer's *Traité des Maladies des Reins*

(1841). This author devoted some 30 pages of fine print to a discussion of the condition in all its manifestations. In 1857 Boogard reported an autopsy finding where "distention of the right renal pelvis was found and the inferior branch [of the renal artery] crossed the ureter near its origin, where a definite pressure was exerted upon the ureter, so that it was obliged to wrap itself around this branch in order to attain the bladder." Thus was an important cause of hydronephrosis—kinking of a ureter around an anomalous vessel—recognized for the first time. Many more years elapsed, however, before full recognition was accorded this pathological condition. In 1894 Fenger described his plastic operation for the relief of hydronephrosis due to constriction by aberrant vessels, and thereafter the urological profession began to turn its attention to the varied causes by which this common lesion may be produced.

Etiology. The fundamental cause of hydronephrosis is some form of obstruction to urinary drainage. It is, therefore, not a disease in itself, but a pathological manifestation common to many urinary-tract affections. The obstructive factor may be (1) mechanical or (2) dynamic, the result of nervous or muscular dysfunction of some part of the urinary tract. The factors causing obstruction are many, and they may occur anywhere in the urinary tract, between the renal pelvis and the external urethral meatus, or they may lie outside the urinary tract. The simple classification of hydronephrosis into congenital and acquired forms, found in many textbooks, is unsatisfactory, because many cases diagnosed as either "congenital" or "acquired" are due to the interaction of both congenital and acquired factors. For example, an anomalous condition, inducing retention and consequent infection, may ultimately be productive of stone, which, in turn, may be the direct cause of hydronephrosis.

Mechanical and anatomical causes of urinary obstruction, which may produce hydronephrosis, are as follows:

Mechanical and Anatomical Causes of Urinary Obstruction

URETHRA:

- Congenital anomalies
- Phimosis (congenital; acquired)
- Pin-point meatus
- Atresia
- Diverticulum (congenital, acquired)
- Congenital posterior urethral valves
- Hypertrophied verumontanum
- Urethrocele

Stricture
Calculus
Tumor
Cysts

BLADDER AND BLADDER NECK:

Congenital anomalies
Contracture of neck (congenital; acquired)
Hypertrophy of neck
Prostatic hypertrophy
Prostatic neoplasm
Median bar
Hypertrophy of interureteral ridge
Diverticulum of bladder
Tumor
Calculus

URETER:

Anomalies of number (bifid ureter, etc.)
Anomalies of termination
Congenital valves and folds
Stenoses
Ureterocele
Atony
Stricture (congenital; acquired)
 Ureteropelvic junction
 Body of ureter
 Ureterovesical junction
Kinks and angulations
Retroperitoneal tumors or tuberculous glands compressing or impinging on the ureter
Pregnancy
Tumor
Stone
Ureteritis and periureteritis
Blood clots

RENAL PELVIC AND RENAL:

Anomalies of the Kidney (form, number, position, size)
Aberrant renal vessels
Ptosis
Stone
Tumor
Renal infection
Aneurysm of the renal artery

Hydronephrotic kidneys are sometimes encountered in the newborn and in young children. It has been widely believed that high insertion of the ureter is the cause of many instances of hydronephrosis existing from birth, but there is a tendency now to regard the elevation of the ureteropelvic junction as a result rather than the cause of pelvic dilatation. Such a hydronephrosis, though essentially "idiopathic" in that no primary cause can be demonstrated, would be increased by postnatal factors, such as calculus-formation, ureteral and pelvic dilatation and injury through stretching and weakening of the muscular structure, or the inflammatory conditions induced by urinary-tract infection. It is a reasonable deduction that the gradual increase in the size of a *congenital* hydronephrotic sac might set up, postnatally, any of the conditions heretofore looked upon as etioloical factors. Valve-formation at the ureteropelvic junction might take place in this way, and high insertion of the ureter, or an anomalous course of an originally normal blood vessel, could readily be explained by these structures having been pushed out of the way of a steadily dilating renal pelvis.

Hydronephrosis may be "acquired" early in life because of defective drainage, this in turn being due to some malformation of the renal pelvis itself, of the ureter, or of the lower part of the tract. Conditions that may produce hydronephrosis early in life are: congenital valves of the posterior urethra (relatively common), congenital stricture of the urethra, marked phimosis, contracted bladder neck, hypertrophied verumontanum, cystic dilatation of the ureter, bilateral stenoses of the ureters, calculus in the urinary tract, lesions outside the urinary tract causing pressure on the ureter (rare in children), spina bifida or other lesions of the central nervous system, and congenital anomalies of the kidney and ureter. Hydronephrosis has also followed ureteral transplantation for the relief of exstrophy of the bladder.

Congenital anomalies of the renal pelvis and ureter play an important part in the production of hydronephrosis in all periods of life. Such anomalies are by no means uncommon. Kretschmer (1937), in a study of 101 cases of hydronephrosis in infancy and childhood, found congenital anomalies of the kidney and ureter in 24, or 23.7 per cent. More than half of these were some form of reduplication of the ureter and pelvis. It is a well-recognized fact that a kidney which is congenitally malformed is more apt to become diseased than a normal organ. Infection usually plays an important part in these cases. Where there is a bifid ureter of any of the various types that may occur, infection is likely to lodge at

the point of union of the two ureters, resulting in a stricture at this point; dilatation takes place above the stricture, both pelves often being affected in cases of double pelves.

Supravesical Obstructions. The chief supravesical causes of obstruction are: (1) strictures of the ureter due to inflammation, (2) calculus, either renal or ureteral, (3) kinking of the ureter due to abnormal mobility of the kidney. (4) aberrant vessels, (5) fibrous bands or adhesions compressing the ureter. The obstruction is most frequently located at the ureteropelvic junction. In 66 cases of non-calculous ureteropelvic obstruction proved by operation at the Brady Foundation, of the New York Hospital, the cause of obstruction was as follows: stricture, 31 cases; aberrant vessels, 29; fibrous bands or adhesions, 18; high ureteropelvic insertion, 6. Frequently, there was more than one obstructive factor present. These conditions are discussed at length elsewhere and require only brief mention here.

Strictures of the ureter are most commonly found at the ureteropelvic junction or at the ureterovesical orifice. They may be congenital or acquired. Inflammatory contraction at the ureteropelvic junction is one of the most frequent causes of hydronephrosis. In many cases in which aberrant blood vessels, renal mobility, or abnormal implantation of the ureter have been assigned as a cause of the hydronephrosis, careful examination of the upper ureter and renal pelvis will reveal inflammatory narrowings which probably have played the primary role.

Calculi are seen frequently in association with hydronephrosis, and are recognized as a common factor in its production. In other cases they are a result of the dilatation, being due to urinary stasis.

Although aberrant vessels have been greatly stressed in the literature as a frequent cause of hydronephrosis, and are discovered as a concomitant feature in many cases, authors differ regarding their importance as primary etiological factors. In congenital hydronephrosis, it is probable that aberrant vessels are a fairly late cause of obstruction, aggravating an already well-developed hydronephrosis. Many observers incline to the belief that while vascular anomalies are sometimes the primary cause of hydronephrosis, more frequently the relation of the aberrant vessel to the ureter necessary for the production of obstruction is the result of altered relations brought about by increasing size of the pelvis and descent of the hydronephrotic kidney, caused, usually, by an inflammatory stricture at the ureteropelvic junction. Distention of the pelvis or ureter may so stretch a normal vessel that it, in turn, becomes aber-

rant. Aberrant vessels can interfere with the peristalsis of the ureter either by pressure or by pulsation.

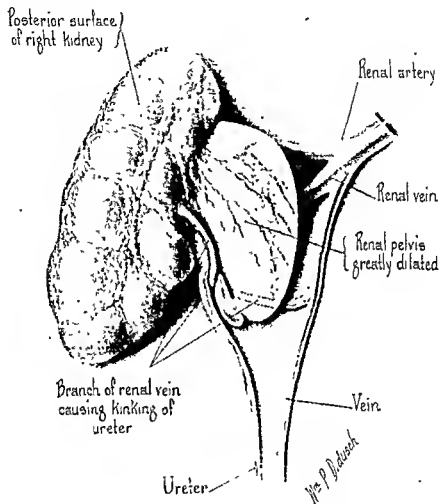


FIG. 309. Hydronephrosis of the right kidney caused by a large aberrant vein which crossed the ureter about 1 inch from the ureteropelvic junction, producing a right-angle kink. Note lobulation of the kidney. Male, aged 11 years.

Fibrous bands and adhesions, by compressing the ureter, may cause hydronephrosis. These are doubtless congenital in some cases, but more often they are due to inflammation in the neighborhood of the affected ureter.

Periureteral fibrosis may compress the ureter and induce backing up

of urine sufficient to cause hydronephrosis. In women, such fibrosis is likely to be seen following gynecological operations or, less often, the use of radiation. The presence of pelvic tumors, cysts, or tuberculous glands may also cause compression of the ureter, with obstruction. In male patients, a not infrequent cause of obstruction leading to hydronephrosis is seminal vesiculitis, which may affect the tissues at the lower end of the ureter so as to cause fibrotic pressure upon it; or the inflammation may even extend into the ureteral and periureteral tissues, resulting in scar tissue and stricture.

Though renal ptosis is common, it is surprising how seldom well-established hydronephrosis is found in association with it. Careful investigation will usually reveal a stricture, constricting band or adhesion, or aberrant vessel, which has acted, with the kinking of the ureter due to the renal ptosis, to produce hydronephrosis. The mere fact that there exists a certain mobility of the kidney does not provide an explanation for hydronephrosis in such an organ (*Movable Kidney*, p. 1617). If, however, there is sufficient ptosis of the kidney to cause kinking of the ureter, or to place the ureter in abnormal relationship to blood vessels (aberrant or otherwise), which are thus enabled to press upon it, there will usually be enough obstruction produced to set up hydronephrosis. Often a ureter thus displaced will be fixed in its abnormal position by adhesions and fibrous bands which frequently are obstructive enough to cause stasis. Depending upon the examiner, the hydronephrosis in such cases may be interpreted as being due to movability, an aberrant vessel, kink, stricture, or fibrous bands or adhesions.

Mathé, who has given special study to renal ptosis, holds that as the kidney gradually descends, the renal pedicle is slowly elongated, letting the kidney fall, although the upper part of the ureter may be held in a relatively normal position by a blood vessel which has chanced to intercept it. This observer has found that back pressure is more likely to take place when the kidney is only slightly movable. When there is great mobility, or the so-called "floating" kidney, the ureter is not likely to become obstructed because the kidney moves away from any aberrant vessel which might impede it, carrying the kidney in the same general direction. Hydronephrosis developing in a ptosed kidney is usually of moderate degree. Superimposed infection, however, may cause dense adhesions between the kink in the ureter and the wall of the renal pelvis or an adjacent renal vessel.

Trauma to the ureter, resulting from external accident (rare), ureteral instrumentation, or from involvement of the ureter in surgery upon neighboring organs, may be the cause of stricture and eventual hydronephrosis. Injury to the nerve ganglia of the ureteral wall will interrupt or inhibit permanently the normal ureteral peristalsis at the point of injury or anastomosis. A certain amount of stasis occurs above the obstruction, and this constant accumulation of urine causes dilatation of the ureter above the point of nerve injury—the dilatation frequently extending all the way to the renal pelvis. Hydronephrosis and hydro-ureter are very common findings in cases of ureteral trauma or anastomosis.

There is probably also an occasional case of congenital neuromuscular defect in the ureteral wall.

Neuromuscular dysfunction within the kidney itself may serve to set up hydronephrosis by much the same mechanism which induces stasis and back pressure in the ureter after injury to its nerve supply. Overstimulation of the sympathetic nerves may bring about spasm of the smooth muscle of which the ureteropelvic "valve" is composed and which surrounds the necks of the major and minor calyces. Such spasm, if it occurs often enough, would quickly institute a hydronephrosis, which would be more or less intermittent in type. If such a spasm be more or less continuous, there will be a generalized increase in the tonus of all the muscles of the pelvis and calyces, and this, in turn, will bring about higher intrapelvic pressure and result in clubbing of the calyces and delay in evacuation of their contents. Von Lichtenberg has emphasized the comparative frequency with which such functional dynamic spastic contraction undoubtedly takes place, even though the condition is not often clinically recognized. He claims that at operation he has repeatedly demonstrated this muscular contraction of the upper ureter, analogous to cardio-spasm or pyloro-spasm, and states that he found it in almost 60 per cent of a series of 80 patients operated upon. Such neuromuscular dysfunction is frequently associated with pyelonephritis.

A rare cause of hydronephrosis is aneurysm of the renal artery, only 74 cases of which have been reported in the literature (Lowsley and Cannon, 1943).

In women, pregnancy, by inducing pressure on the ureters, commonly causes obstruction and dilatation.

Infravesical Obstruction. The chief infravesical factors in the production of hydronephrosis are obstructive lesions of the bladder neck

(prostatic hypertrophy, prostatic neoplasm, contracture, median bar). Obstruction to drainage may also be caused by bladder tumor, stone, or diverticulum, as well as by lesions below the bladder neck, such as congenital valves of the posterior urethra, urethral stricture, diverticu-

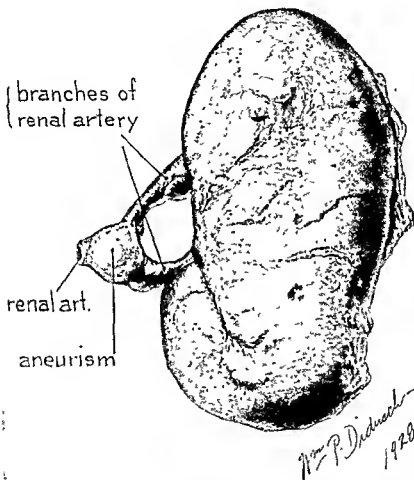


FIG. 310. Aneurysm of the renal artery. Gross specimen. (Christeller.)

lum, tumor, or stone, or pin-point meatus. The hydronephrotic condition is usually bilateral, although the extent of dilatation may vary on the two sides. The appearance of the ureters and renal pelvises in a long-standing case of congenital valvular obstruction in a young child resembles that in advanced prostatism.

When the obstructive lesion is situated at the bladder neck or below it, the bladder, by a compensatory hypertrophy of its wall, is able for some time to empty itself fairly completely. The kidneys are thereby protected from injury. As the obstruction increases, however, the bladder finds it increasingly difficult to empty itself. The retained urine increases in amount and becomes infected. Small cellulæ form between the hypertrophied muscle bundles of the bladder wall, and, as the thinning of the wall progresses, a diverticulum (or several) may form, which may attain the size of the bladder itself. If the obstruction is not removed, back pressure on the ureters and kidneys will cause dilatation of these structures, with the ultimate production of hydro-ureter and hydronephrosis.

Pathology. The changes which occur within the renal pelvis and parenchyma as a result of blockage of the renal drainage system are essentially similar, whether such stoppage be partial and intermittent, or continuous up to complete occlusion of all outflow.

When there is complete blockage at the ureteropelvic junction, or anywhere in the ureter, the pelvis rapidly becomes distended with urine, and the entire kidney soon suffers pressure atrophy. If the original hydronephrotic collection is not promptly reabsorbed, there may be secondary atrophy or a general shrinkage of the renal tissue, and marked circulatory changes will be in evidence.

It is obvious that if the secreting portion of the kidney continued to function unabated, but complete blockage of its outlet has taken place, there must be some way of equalizing intrapelvic pressure; otherwise rupture would occur within a short time. As a matter of fact, rupture of a hydronephrotic sac is a rather rare accident and is seldom spontaneous, being commonly the result of external violence or muscular strain. Atrophy is the regular outcome of excretory back pressure, but there must be a counterplay between urinary secretion and pelvic absorption at such rates as to permit secretion to continue and yet maintain an intrapelvic pressure sufficient to produce the effects known as hydronephrotic atrophy (Hepler).

The results of his experiments to determine the importance of back pressure in the production of hydronephrosis have been summarized by Hinman as follows:

Excretory back pressure is an essential factor in the production of hydronephrotic atrophy. Its effect is linked closely to nutritional disturbance. Atrophy is more of the anemic than of the pressure type. A relative increase of ischemia, whether general or local, causes a more rapid dilatation and atrophy even with a lower back pressure. Increasing secretory pressure alone does not affect the ordinary rate of

development. Back pressure is not the controlling factor. A complicating renal infection may modify it markedly, even producing a complete anuria. Hydro-

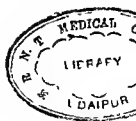
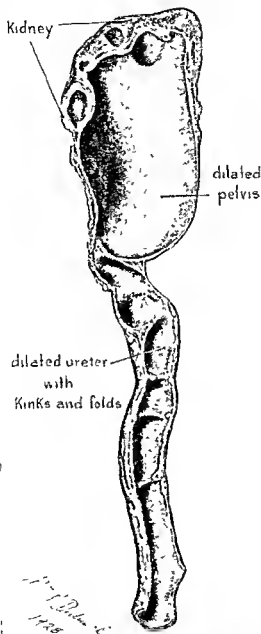


FIG. 311. Hydronephrosis and hydro-ureter following a gonorrheal stricture of the urethra. (Christeller.)

nephrosis cannot develop with anuria, and any cause of anuria, therefore, would prevent the development of hydronephrosis.

The routes of absorption, which permit the continuance of the hydronephrotic condition, are of prime pathological importance. Experimentation has shown that there are two main routes: (1) through the tubular system, and (2) by way of the lymphatics.

It is evident that urinary back pressure must have its most potent effect upon the blood vessels of the portion of the kidney directly affected, and that nutritional disturbance is produced by this pressure upon the vascular structures. Robbed thus of their blood supply, the tissues of the pelvis and renal parenchyma will soon dilate and atrophy. Dilatation will not be confined to the pelvis, but will soon extend to the tubes, and will react upon the peritubular vessels, resulting in compression and thinning out of the arterioles and their tributaries, and still further disturbances in nutrition and diminution of function. With prolonged back pressure, all the vascular tissue will disappear, and in the attenuated sac which finally remains it will be impossible to find any structure of recognizable form except a few glomeruli.

Though the mechanism of hydronephrotic atrophy and the parenchymal changes, as seen microscopically, are identical under all circumstances, the macroscopic appearance presented by the renal tissue varies in accordance with the character and location of the obstruction originally responsible. In early cases, in which the obstruction is low down, there is frequently compensatory hypertrophy and dilatation of the ureter, and less blunting of the calyces than is the case when the obstruction is at the ureteropelvic junction. The position of the pelvis in relation to the rest of the kidney is also important. If the pelvis is of the intrarenal type, the dilatation is likely to be mostly intrarenal and at the expense of the parenchyma. If the pelvis is of the extrarenal type, the distention will be largely outside the organ, atrophy of the parenchyma taking place later.

Infection is always an important factor, for a sterile hydronephrosis may at any time be converted into a pyonephrosis, which will exert a profoundly toxic effect upon the entire system, and this, in turn, will react upon the urinary tract. An infected hydronephrosis is much more difficult to treat than one which has remained sterile, and when surgical intervention is imperative, the prognosis will be greatly influenced by the type and extent of associated infection.

Dilatation of the ureter and renal pelvis occurring during pregnancy has already been referred to. The kidney in pregnancy presents conditions peculiar to that state, which, though not properly termed "patho-

logical," are yet so far from the normal non-pregnant state that they must be regarded as pathological alterations (Pyelonephritis of Pregnancy, p. 1474).

Symptoms. Hydronephrosis gives no typical symptom-complex, as is evident from a consideration of its etiology. Sometimes the symptoms are those of the pathological condition responsible for the development of the hydronephrosis (stone, ureteral stricture, movable kidney with kink, obstruction at or below the vesical neck, etc.). In other cases, the clinical picture is that of acute or chronic pyelonephritis, or of chronic nephritis. Frequently the hydronephrosis, though of marked degree, may be symptomless until the onset of secondary infection. Occasionally the hydronephrosis runs an apparently silent course and is discovered only on routine urological examination. Again, the general symptoms may completely dominate the clinical picture, delaying discovery of the urinary pathology until irreparable damage has been done to one or both kidneys.

Hydronephrosis due to infravesical obstruction is of the bilateral type. Unless infection has occurred, the renal condition is commonly silent, the clinical picture being that of vesical neck or urethral obstruction. When infection sets in, the clinical picture of acute pyelonephritis is added to the vesical symptoms. Symptoms of kidney involvement in the early stages are similar to those of chronic nephritis. The illness is of a general nature and may be very insidious and difficult to diagnose without a complete investigation. As nephritis may co-exist with obstruction, it is essential in patients with symptoms of nephritis—particularly elderly men—to determine definitely whether the symptoms are due to nephritis, or obstruction, or both. In infants, an abdominal tumor, incontinence, and constitutional uremic symptoms are suggestive of bilateral hydronephrosis due to obstruction in the lower tract.

Hydronephrosis of supravescical origin is unilateral as a rule. When the stone, stricture, kink, adhesions, or pressure from tumors or pregnancy is bilateral, obviously both kidneys will be affected. Owing to the presence of one healthy kidney, which can carry on the necessary excretory function, a unilateral hydronephrosis may progress unchecked to an enormous size. Unless there is severe secondary infection, the symptoms in the unilateral cases are less likely to be general than in bilateral involvement, but arise chiefly from the pressure of the tumor.

Irrespective of its cause, the chief symptoms of hydronephrosis are

pain in the back, with or without tumor, increased frequency, and pyuria and other symptoms of infection. The pain may be a constant, dull ache, which may be referred to the umbilical or other neighboring regions. More often it is of the colic type, and may recur frequently. In between the attacks the patient may feel fairly well. The pain may be associated with tenderness at the costovertebral angle. Tumor is sometimes the first indication of hydronephrosis, or it may not be detectible until the pain has become very severe, or it may be absent altogether. The tumor may be larger at one time than another, and moves with respiration. The pressure exerted by a hydronephrotic kidney on the surrounding tissues may induce circulatory and intestinal symptoms; in fact, gastrointestinal symptoms are not infrequently the predominant manifestations of a hydronephrosis.

Urinary symptoms are inconstant and often lacking. The most common urinary symptom is increased frequency of urination. Often, following an attack of pain, there may be a copious flow of urine, due to temporary relief of the obstruction. With attacks of renal or ureteral colic due to calculus, there is frequently associated hematuria. Hematuria may also occur without stone, but this is uncommon.

When infection is superimposed upon the hydronephrosis, constitutional symptoms are added: chills, fever, loss of weight, malaise, headache, nausea and vomiting, and general septic poisoning.

Diagnosis. With our present means of examination, the presence or absence of hydronephrosis can be established beyond doubt. Nevertheless, as every urologist knows, this condition frequently progresses to a marked degree before it is discovered. The reason, as we have seen, is that hydronephrosis is often symptomless until a secondary infection supervenes, and the history and preliminary study may give no presumptive evidence of its presence. If the possibility of hydronephrosis is borne in mind in those cases in which there is a history of recurring attacks of pyelitis, as well as in cases of persistent pyuria which fail to respond to proper medical management, and in cases with a long-standing history of symptoms indicating obstruction at or below the bladder neck, the proper diagnosis could be made more frequently and at an earlier stage of the disease than it has in the past. Indeed, it is hardly too much to say that hydronephrosis requires consideration in practically every case of genito-urinary disease, since back pressure—the essential cause of hydronephrosis—is a very common effect of urogenital anomalies and disease.

The diagnosis of hydronephrosis requires a consideration of the whole urogenital tract, since it is essential to determine not only the presence of a hydronephrosis, but also the nature and location of the obstruction responsible for the condition, the presence of secondary factors, and the extent of damage to the kidneys. This requires a complete urological investigation, namely, a carefully elicited history, thorough physical examination, and the combined employment of cystoscopy, ureteral catheterization, bacteriological and cytological examination of the urine, renal functional tests, and pyelography.

The ordinary clinical examination may or may not give presumptive evidence of hydronephrosis. Physical examination may reveal a tumor in the kidney region which, while not pathognomonic, when correlated with other findings is diagnostically significant. The observation that the tumor has varied in size from time to time is important. The physical examination in small hydronephroses is negative.

The lower urinary passages must be carefully examined for the presence of strictures, prostatic enlargement, posterior urethral valves, or other causes of obstruction. If obstruction is found, investigation of the upper tract becomes necessary, to determine the extent of damage by back pressure and the presence or absence of secondary contributing factors.

Of the special means for the establishing of a positive finding of hydronephrosis, ureteral catheterization and pyelography are the most useful. When inserting the ureteral catheter, it is important to watch the efflux of urine from the end of the instrument. Normally the urine drips from the catheter a few drops at a time; but if the end of the catheter lies in a hydronephrotic sac, the flow of urine will commonly be continuous and copious.

Renal functional studies are of great importance in hydronephrosis, but, unless they are thoroughly established, may easily be misleading. Of particular importance are the tests for relative function, urea concentration, and the estimation of blood urea.

The plain x-ray film, aside from showing changes in the kidney outline and stones when present, furnishes little diagnostic information. Pyelography, however—both retrograde and excretory—yields valuable information in this group of cases, not only in disclosing the anatomical condition, but also in revealing the nature and location of ureteral obstructions, disturbance of dynamics, or changes of tonus. The commonly accepted pyelographic proof of hydronephrosis is the finding of

dilatation of the renal pelvis, together with blunting of the minor calyces. Later the minor calyces tend to coalesce, the major calyces become club-like, the pelvis increases in size, and there is considerable modification of the ureteropelvic angle.

The value of serial pyelograms in hydronephrosis was reported on by Henline and Bray, of the Brady Foundation, in 1937. Although single pyelo-ureterograms are sufficient for the demonstration of some pathological conditions of the kidney and ureter, they can seldom be relied upon for the recognition of strictures, kinks, atony of the ureter, and certain other abnormalities which have an important bearing on the production of hydronephrosis. In the diagnosis of these conditions constancy is a factor of the greatest importance. Kinks and apparent distortions at the ureteropelvic junction, which in a single urogram appear to be obstructive, may be absent in a second urogram or proved to be non-obstructive with serial x-rays.

In the study of hydronephrosis, serial pyelograms are of value in revealing not only the site and nature of the obstruction, but delayed emptying of the renal pelvis—the initial stage of hydronephrosis. Excretory urograms are frequently helpful in determining the emptying time with marked obstructions, but a clear demonstration of the pelvis and calyces is seldom obtained in early hydronephrosis. Serial pyelograms, taken at varying intervals following retrograde pyelography, permit the diagnosis of even early obstructive lesions. Occasionally it will be found that cases showing little or no evidence of pyelectasis or ureterectasis in the original pyelogram will reveal markedly delayed emptying time, with no evidence of contrast material in the ureter in the delayed films.

Serial pyelography is discussed more at length under *Roentgenography of the Genito-Urinary Tract* (p. 133).

Prognosis. The outlook in any case of hydronephrosis depends upon (1) the stage of the condition at which treatment is instituted, (2) whether or not infection has supervened, and (3) the underlying cause of the hydronephrosis. An early sterile hydronephrosis can usually be drained, and if the contributing obstructive factors are eliminated, the kidney often recovers its original efficiency. Unfortunately, many patients come under observation late in the course of the disease, when advanced destruction of the kidney has occurred, making nephrectomy necessary.

Treatment. The treatment depends upon (1) the underlying contributing factor or factors, (2) whether the hydronephrosis is early or advanced, (3) whether there is associated infection and, if so, its extent, (4) whether the condition is unilateral or bilateral.

Obstruction and infection being the primary causes of hydronephrosis, the paramount objective in the treatment of hydronephrosis is their complete and permanent correction.

In hydronephrosis resulting from infravesical causes, the treatment is removal of the obstruction in the lower urinary tract as quickly as possible. The hydronephrosis in these cases is usually bilateral. With removal of the obstruction, the kidneys will begin to function normally in so far as permanent damage to their structure permits. If the renal impairment has not been too excessive or too prolonged, the patient has an excellent chance of recovery. In these cases, if the obstruction has been of long duration, there will frequently be found secondary obstructive factors which also must receive consideration. These may occur in either the lower tract, the bladder, or the upper tract. Such secondary factors include acquired diverticula, hypertrophy of the trigone, angulated hydro-ureters, stone, stricture at the ureteropelvic junction, etc.

In hydronephrosis of supravescical origin, the first point to be determined is whether the condition is unilateral or bilateral. When dealing with an early unilateral hydronephrosis due to stone, stricture, kink, or other cause of obstruction, the freeing of the obstruction, by either urological dilatation of the ureter and lavage, or by a strictly surgical approach, frequently proves successful. Many patients, however, will be found to have passed beyond help from these conservative measures. Nephrectomy is often necessary for a painful, functionless or poorly functioning kidney, or for a seriously infected kidney with moderate impairment of function.

In hydronephrosis dependent upon a ureter kinked by the abnormal position of its kidney, splinting of the ureter by the insertion of a catheter, which then passes freely to the renal pelvis, will be followed immediately by a gush of urine, with rapid reduction in the size of the distended organ. Occasionally a ureter so straightened will not again become occluded, but more often, on withdrawal of the catheter, the ureter will again kink and the hydronephrotic sac refill. A slightly mobile kidney is frequently retained in place by a properly fitted belt, but in many cases surgical fixation of the kidney is necessary.

Plastic repair of unilateral hydronephrosis should be done only when function has been found to be good or potentially so, and when the kidney is not too badly infected. The various types of plastic procedures applicable to the surgical repair of hydronephrosis of ureteropelvic origin have been described under Surgical Treatment of Non-Calculous Obstructions at the Ureteropelvic Junction (p. 1305).

Hydrocalyx

"Hydrocalyx" is the term applied to dilatation of a single renal calyx without concomitant dilatation of the remaining calyces. It is due to obstruction or stricture of the infundibular portion of the calyx, or, according to K. H. Watson, in the absence of apparent obstruction, to achalasia at the neck of the calyx or at its junction with the pelvis. Dilatation of a single calyx which is not due to ulceration or calculus-formation is uncommon. However, even in the absence of stone, a distended calyx may produce symptoms of retention, or retention and infection, of varying severity. The most common symptom is pain in the loin on the affected side; this may take the form of a constant dull ache, or paroxysms of sharp pain, or a persistent dull ache with intervals of acute pain.

Beneventi, in a recent review of the literature, found the condition to occur in the third decade of life "with almost constant regularity." He states that it must be differentiated from (1) calyceal diverticulum—a dilated cavity distal to and not a part of the calyx but connected to the calyx by a small channel; (2) a renal cyst which has ruptured into the pelvis, and (3) the calyceal dilatation or "clubbing" occurring in the course of pyelonephritis—called "localized obliterating pyelonephritis" by Hyams and Kenyon.

Treatment. The treatment of hydrocalyx has been either by nephrosotomy, with dilatation of the infundibular stricture, or by calyceal resection. Beneventi, however, believes that open operation is not always necessary; that in some instances—particularly where the superior calyx is involved—it is possible to relieve the patient by retrograde dilatation of the infundibular stricture. A patient with a large dilatation of the superior calyx of the right kidney, with a definite stricture of the infundibulum, thus treated by him has been kept symptom-free for almost two years. During this period the hydrocalyx has substantially decreased in size, repeated tests have shown the renal function to be normal, and urine cultures have shown no growth. The dilatations must be done at fairly frequent intervals and may have to be continued over a considerable period of time. Beneventi's patient had dilatations every three weeks for about nine months; he was then given a rest period of nine months, during which he experienced none of his previous pain and enjoyed good health.

"Medical" Diseases of the Kidney (Nephritis and Nephrosis)

"Medical" diseases of the kidney, as opposed to the so-called surgical group, include those pathological conditions which cannot be definitely attributed to direct invasion of the kidney by bacteria, or to anomalies, obstruction and stasis, trauma, stone, cyst, or new growth. In the former (grouped as Bright's disease) the pathological change may be proliferative, necrotic, or sclerotic, and is due to injury caused by extra-renal bacterial toxins, chemical injury, or metabolic alterations.

Probably no subject in medicine has caused greater difficulty in classification than that of Bright's disease. The chief difficulty has always been the correlation of the various clinical types with the greatly diversified postmortem appearances. Perhaps the most influential of the numerous classifications that have been put forth has been that of Volhard and Fahr (1914). The classifications of Elwyn, Cruickshank, and, especially, Addis, though admittedly deriving from Volhard and Fahr's, have the merit of greater brevity and clarity, and will be followed in the present brief consideration of the subject.

Any system of classification must take into account the fact that most lesions of Bright's disease are composite in nature, affecting more than one part of the kidney substance and producing symptoms referable to different portions of the renal structure. The structure of the kidney is extremely complex, despite the fact that it consists of but three main elements: (1) the vascular structure, which, in addition to the renal arteries and veins, includes the glomerular tufts, (2) the interstitial tissues, (3) the epithelial tissues, including Bowman's capsule and the membranous lining of the renal tubules. Bright's disease may attack any one or all of these structural elements. A given lesion is designated "glomerulonephritis" when it primarily affects the glomeruli, "interstitial nephritis" when it primarily affects the connective tissue, and "tubular nephritis" when it chiefly involves the tubules; but in most cases one or both of the other structural elements are more or less affected secondarily.

From a pathological standpoint, three different types of lesions are to be distinguished in Bright's disease: (1) hemorrhagic or inflammatory, (2) degenerative, and (3) sclerotic. Only one type of lesion may be present, or two, or all three may overlap

*Classification of Nephritis and Nephrosis***A. Hemorrhagic (inflammatory) types**

1. Acute diffuse glomerulonephritis
2. Subacute diffuse glomerulonephritis
3. Chronic diffuse glomerulonephritis

B. Degenerative types (nephroses)

1. Pregnancy nephrosis
2. Lipoid nephrosis
3. Amyloid nephrosis
4. Chemical nephrosis

C. Sclerotic types

1. Arteriosclerosis of the renal artery and its larger branches ("senile" kidney—clinical picture not characteristic)
2. Renal arteriolosclerosis (of Elwyn), without renal insufficiency, with the clinical syndrome of benign hypertension
3. Renal arteriolosclerosis, with renal insufficiency
 - a. Malignant form of renal arteriolosclerosis
 - b. Malignant form of hypertension

D. Mixed types*(1) Hemorrhagic (Inflammatory) Nephritis*

Acute Diffuse Glomerulonephritis. Acute glomerulonephritis is a diffuse, bilateral inflammation involving principally the glomeruli, with secondary changes in the tubules. It is characterized by the presence of casts and abnormal quantities of red blood cells in the urine, and is due to the injurious effects of extrarenal bacterial toxins, particularly upon the glomerular capillaries. Glomerulonephritis follows many different kinds of extrarenal infections (focal, respiratory, the exanthemata, etc.), but differs entirely from the varieties of nephritis and pyelonephritis which are caused by direct bacterial invasion and which also follow extrarenal infections, usually staphylococcal and streptococcal infections of the skin or upper respiratory tract. It also differs from the renal inflammation occurring at the height of infectious fevers.

Pathology. The lesions of acute diffuse hemorrhagic glomerulonephritis primarily involve the glomerulotubular tissues, though pathological changes also occur in the interstitial elements, epithelium, and blood vessels. The kidney is larger than normal and usually edemic, but outwardly shows comparatively little abnormality. The capsule strips readily. The surface beneath will be found to be more or less hemorrhagic and congested, with actual areas of hemorrhage often

observable even before the cortex has been exposed by sectioning. The cortex is swollen and well marked off from the medulla, the grayish glomeruli standing out distinctly from the cortical tissue, which is of a brownish hue. The tints are those of congested tissues anywhere, but will vary according to the degree of congestion.

Symptoms and Diagnosis. As a rule, the diagnosis is not difficult. The characteristic symptoms and signs are renal insufficiency, edema, hypertension, and blood, casts, and albumin in the urine. However, only one or two of these may be present, and the differential diagnosis may then be difficult. The onset of glomerulonephritis may be acute or insidious. Mild forms have been described, characterized by albuminuria, microscopic hematuria, and casts, which eventually progress into the classic picture of gross hematuria, hypertension, and edema. Some observers believe that the fact that so many patients with chronic nephritis have no history of an acute attack may indicate that the initial stage was so mild as to be unrecognized, and that nephritis was not suspected until urinary abnormalities were discovered at a later date. If the onset is very acute, the attack may at first resemble an acute infection, with elevated temperature, chills, and vomiting.

Prognosis. Many patients recover; but if the extrarenal factor continues, subjecting the kidney to constant or repeated intoxications, the inflammatory reaction in the kidney may persist or suffer exacerbations and result in a subacute, subchronic, or chronic form of diffuse glomerulonephritis.

Subacute Diffuse Glomerulonephritis. The clinical manifestations of subacute diffuse glomerulonephritis do not differ materially from those of the acute form; in fact, it may be difficult to decide whether one is dealing with a mild acute attack or with an unusually active but nonetheless subacute glomerulonephritis which is likely to progress to complete renal collapse unless appropriate therapeutic measures are promptly instituted. Many writers make a distinction between subacute and subchronic forms. Of the latter it need merely be said that they last longer and run, on the whole, a milder course, although they usually end fatally in from 1 to 3 years, whereas the fatal termination is more rapid in the subacute cases.

Pathology. In the subacute form the kidney is soft and enlarged. The capsule strips easily, showing a pale, smooth under surface, mottled with grayish streaks and scattered over with yellowish spots, which are fat deposits or petechial hemorrhages. The glomerular changes may

be extracapillary or intracapillary. In the extracapillary form the capillary tufts are not enlarged, but are pale and ischemic in appearance. Masses of epithelial cell debris fill the capsular spaces outside the tufts. Later there may be hyalinization of the glomerular loops, with the entire glomerular area converted into a structureless mass surrounded by a thickened and degenerated capsule. In the intracapillary form there is enlargement of the individual glomeruli. The capillary tuft fills the capsular space because the loops have swelled, and the glomerulus itself has become infiltrated with an exudate in which the microscope can demonstrate leukocytes and endothelial-cell proliferation. According to Cruickshank, the views of Volhard and Fahr—namely, that there is a direct connection between the relative proportion of extracapillary and intracapillary glomerulitis and the rate of progress of the clinical signs of renal impairment—have found wide acceptance by both American and European authorities:

Predominance of extracapillary glomerulitis is found in those cases of subacute nephritis which terminate fatally within a few months of their onset. Throughout their course these cases exhibit clinical signs something like those of acute nephritis. On the other hand, if there is a predominance of intracapillary glomerulitis there is believed to be less interference with renal function, at least in the earlier stages, and the clinical manifestations are more like those of chronic nephritis. These cases, with their slower course and more gradual progress toward complete failure, are distinguished from the other variety by the use of the term "subchronic."

The tubular and interstitial changes correspond in distribution and intensity to the lesions of the glomeruli. If the destruction of the glomerulus is complete, there will be equal destruction of its tubule. Tubules which are not completely destroyed will usually be distended and show partial destruction of their epithelium, with areas of fat and hyalin degeneration in the remainder (see Nephrosis, p. 1429). Irregular deposits of fibrosis, with cellular exudation and fatty degeneration, can be made out in the interstitial tissue, while hyalinization and perivascular fibrosis characterize the intima of the veins and arterioles.

Symptoms and Diagnosis. As the subacute and subchronic forms of diffuse glomerulonephritis are progressive stages of the acute form, the clinical manifestations will be essentially similar: edema, changes in the composition of the urine, hypertension, and altered blood findings.

Edema, though a regular feature, may arise from several different causes. It may be due to cardiac insufficiency; or the edema, as in acute glomerulonephritis, may affect the serous cavities as well as the sub-

cutaneous tissues; or the fluid may have the "milky" appearance characteristic of lipoid nephrosis. The fact that the edema is so often of the nephrotic type may convince the examiner that he is dealing with a nephrosis instead of a subacute nephritis. Many cases probably actually present elements of both the nephritic (inflammatory) and the nephrotic (degenerative) stages.

Albumin, while never absent from the urine in subacute nephritis, may vary considerably in amount. Hematuria is present, as in the acute form, but the blood may range in amount from a few red blood corpuscles to an amount sufficient to produce urine of a deep mahogany color. The specific gravity also varies, but remains low as a rule, even when the total amount of urine voided is greatly reduced. The centrifuged sediment shows, in addition to leukocytes, red blood cells, and epithelial debris, a wide variety of casts, mostly hyaline and granular.

The cardiovascular picture in renal disease is sometimes so emphasized that the renal condition will be neglected or unnoticed. When kidney disease has been present for some time, there is usually considerable cardiac hypertrophy, and the symptoms may closely simulate those of mitral disease. Later, when both heart and kidneys fail, the well-recognized symptoms of dyspnea, cyanosis, and syncope supervene.

The hypertension of the subacute form of nephritis does not differ from that of the acute type—from 40 to 60 mm. Hg over the figures normal for the particular patient being about the average. Toward the end, however, when renal failure begins to be evident, the blood pressure may descend to practically normal.

With increasing renal dysfunction, there will be a rise in the non-protein nitrogen content of the blood. Kidney insufficiency is evidenced by an increase in the blood urea, the creatinine, and the classic sign of the older clinical school—uric acid. When renal insufficiency increases rapidly, the volume of the blood plasma will be somewhat greater, but the red blood cells and the hemoglobin will be proportionately reduced, though the volume of leukocytes remains normal or but slightly above. Many Bright's disease victims are markedly anemic.

The ophthalmological signs of renal disease are important, and the progress of the disease may often be watched by inspection of the eye grounds. The chief eye signs are edema and choking of the disc, hemorrhage into the conjunctiva, and, in the later stages, sclerosis of the vessels of the retina.

Uremia is typical of chronic rather than subacute glomerulonephritis,

but the milder manifestations of uremia—nausea, vomiting, stupor, and muscular spasm—may be in evidence during the subacute course.

Prognosis of Subacute Glomerulonephritis. The prognosis of the subacute form, unlike that of acute glomerulonephritis, is uniformly poor. The disease is progressive, and frequently terminates fatally in from 3 to 6 months.

Chronic Diffuse Glomerulonephritis. Like all chronic processes, chronic glomerulonephritis has its origin in an acute attack of the same pathological process. The first appearance of the renal affection may have been insidious and the condition have remained unrecognized until chronicity was well established. This is rare, however. Usually the acute phase is recognized and treated; and its subsidence into the subacute or chronic form takes place despite every effort to stay the progress of the disease.

Pathology: Symptoms: Diagnosis. What has been said regarding the pathology and symptoms of the acute and subacute forms applies here also. All the symptoms are accentuated in so far as they show an increasing trend toward renal failure. There is an increase of protein in the urine, though this can be controlled to some extent by careful dieting. Hematuria is increasingly frequent, and edema is a constant feature. Blood pressure rises and falls, but tends constantly to remain at higher levels. When the blood pressure reaches the stage where it is permanently elevated, the chronicity of the disease is definitely established. Signs of renal insufficiency are increasingly evident. There is sometimes an increased output of urine of low specific gravity, but, in general, the urinary secretion diminishes steadily. Most striking in the chronic syndrome are the effects of cardiovascular hypertrophy and of generalized arteriosclerosis, which regularly accompany the persistent rise in blood pressure and the steady extension of the inflammatory and degenerative processes going on in the kidneys. To the symptoms previously listed—headache, nausea, dyspnea, gastrointestinal symptoms, etc.—must be added, at this stage, nasal hemorrhages and certain subjective manifestations, such as tinnitus aurium, disorders of the sensory nerves, excessive fatigue upon slight exertion, and a general slowing of physical and mental ability—all continuing in the downward course toward the inevitable termination, when renal insufficiency eventuates in complete renal failure.

The amount of urine excreted remains fairly satisfactory so long as the heart continues compensated; but when cardiac failure begins, oliguria

sets in, and thereafter the urine typical of cardiac failure will be produced—loaded with protein and carrying a heavy deposit of both organized and unorganized elements. When cardiac failure is added to renal failure, no tests of renal function will be necessary to establish the imminence of the uræmic state (see *Uremia*, p. 1436).

Prognosis of Chronic Diffuse Glomerulonephritis. The victim of chronic Bright's disease may, and usually does, live for years in more or less acute discomfort; and because his affliction follows so slow and drawn-out a course, reducing his vitality and making him peculiarly susceptible to any infection with which he may come in contact, he often dies of an intercurrent ailment. But even harring such accident, the termination is uniformly fatal.

(2) *Nephrosis*

The term *nephrosis* includes a variety of conditions in which degeneration of the epithelium of the renal tubules is the principal feature. The degeneration ranges in degree from simple cellular changes of the tubular epithelium to complete and widespread destruction. Under this designation may be grouped not only lipid nephrosis, amyloid kidney, the toxic nephrosis of pregnancy, and chemical nephrosis, but also hyaline, fatty, and necrotic changes occurring during the course of Bright's disease.

Some of these degenerative changes, like lipid nephrosis, are easily distinguished, while others are vaguely defined and cause much difficulty in differential diagnosis. The hemorrhagic and inflammatory form of Bright's disease often combines a necrotic element, and in some sclerotic cases degenerative changes take place in the tubular epithelium and, to a less extent, in the glomeruli as well. These degenerative processes have symptoms characteristic of themselves, and differing from those regularly seen in the better understood types of Bright's disease. Thus, in a single individual one may see clinical evidences that both nephritis and nephrosis have occurred, or one may see renal sclerosis and nephrosis in the same patient. In these "overlapping" cases diagnosis may be very difficult.

Etiology. The various types of nephrosis may be due to metabolic alterations, or to chemical poisoning or bacterial intoxication. "The pathogenesis of nephrosis is complex and obscure, but appears to be associated with general disorders of metabolism so that renal influences are secondary rather than primary causes in the development of its clinical manifestations" (Cruickshank).

Pathology. The lesions of nephrosis are almost exclusively degenerative in type. They comprise cloudy and hydropic swelling, hyaline, fatty, granular, and lipid degeneration, as well as amyloid and calcareous infiltration. These lesions vary within very wide limits. The degeneration affects primarily the tubular epithelium, particularly that of the convoluted tubules. Along with degeneration, the microscopist can frequently observe signs of cellular regeneration in the form of flat cells, resembling endothelium, directly beneath the degenerated elements. Changes are not, as a rule, noted in the glomeruli or collecting tubules until the disease has made considerable progress. When glomerular changes occur, they are degenerative rather than inflammatory in type.

Lipoid Nephrosis. Lipoid nephrosis is a chronic type of parenchymal degeneration, showing distinctive and well-marked changes, namely, major involvement of the proximal convoluted tubules, which, microscopically, show a deposit of fat and lipid in the cells. Lipoid nephrosis may occur alone, or in combination with diffuse glomerulonephritis, or with amyloid degeneration of the kidney. When it occurs together with chronic glomerulonephritis, we have the condition called "chronic parenchymatous nephritis" by the older generations of renal therapists.

Pathology. The greatest alteration is seen in the proximal convoluted tubules. The distal convolutions and Henle's loop are usually less prominently involved, while the collecting tubules are seldom materially changed. The tubular alterations take the form of dilatation, with flattening of the lining cells in some areas, while in others the cells are so swelled as partially to occlude the tubule's lumen. Much fat is deposited in the cells in any form of nephrosis. So much lipid material may be present as practically to fill the cell-body, and, if a fat solvent is employed in staining, the cells will present a vacuolated appearance. Frequently the cell nuclei will have necrosed entirely. The lumen of the tubule may be filled with detritus—casts, granulations, and desquamations of the injured epithelium. The interstitial tissue is edematous and contains irregularly distributed lipid deposits and areas of infiltration consisting of lymphocytes and leukocytes. In cases of long standing some of the tubules may be completely destroyed and replaced by connective tissue containing lipid deposits. As a rule, there is little change in the vascular elements, though occasionally thrombi may form in the atheromatous areas, the high fibrinogen content of the blood being probably the cause of this thrombotic tendency.

Symptoms and Diagnosis. Lipoid nephrosis is characterized by an insidious onset, a chronic course, edema, albuminuria, oliguria, and

changes in the proteins and lipoids of the blood. The beginnings of the disease are seldom noticed, the onset being so insidious that the patient, when giving a history, is often ignorant of even the approximate date. He can readily tell when he first noticed the "dropsy," for this outstanding symptom constitutes the disease itself in the minds of most laymen. General symptoms, headache, malaise, and anorexia accompany the edema. A loss of weight is frequently masked by the accumulation of water in the tissues, for as soon as the edema can be controlled the patient will be seen to be greatly emaciated.

The renal function is not often impaired, so far as can be ascertained by the results of the blood-urea clearance and urea-concentration tests. The water-excretion test will, however, show that the kidney is mechanically deficient.

Because of the edema and albuminuria, differential diagnosis from glomerulonephritis, in which these symptoms are also prominent, may be difficult in some cases. Some authors, notably Fishberg, lay great stress upon the blood changes as important diagnostic criteria. Well-marked hematuria, according to this author, does not occur in chronic nephrosis, and in the differential diagnosis from glomerulonephritis the fact that red blood cells are completely absent, or present in very small amount, is an important diagnostic sign.

These blood changes involve primarily the colloids of the plasma with less striking alterations in the crystalloids. The abnormalities in the plasma colloids evidently result from the loss of protein in the urine and are identical with those found in other diseases with copious and protracted albuminuria, namely, the nephrotic type of glomerulonephritis and amyloid nephrosis. The loss of blood proteins in these conditions, combined with the efforts of the body to regenerate the proteins and perhaps to compensate in other ways for their loss, produces characteristic changes in the proteins, fats, and lipoids of the plasma. The resulting "nephrotic blood picture," as it may be termed, consists essentially in the following:

1. Decrease in the total protein content of the plasma, largely at the expense of the albumin fraction, with resultant inversion of the albumin to globulin ratio.
2. Increase in the fibrinogen content of the plasma.
3. Decrease in the colloid osmotic pressure of the plasma.
4. Increase in the velocity of sedimentation of the red blood cells.
5. Increase in the concentration of fats and lipoids in the plasma.

In lipid nephrosis there is such a degree of lipemia as to give a distinctly "milky" appearance to both serum and plasma, and the hypercholesterolemia, so characteristic of nephrosis in general, is always to be noted.

Prognosis. The prognosis is uniformly poor. The disease often lasts

for years, but is inevitably fatal. This termination depends upon whether it occurs by itself, or in combination with chronic nephritis or with amyloid disease (Elwyn). In cases with amyloid disease, the primary lesion responsible for the amyloid changes determines the outcome of the lipoid nephrosis. In the cases with glomerulonephritis, death will be due to renal failure unless the patient's life is cut short by an intercurrent affection. The most common fatality, however, is a pneumococcus peritonitis, especially if the patient is a child. Such a complication may follow influenza or bronchitis, or may occur separately. Exposure of these patients to diphtheria, erysipelas, or other acute infections is almost invariably fatal.

Amyloid Nephrosis. Amyloid nephrosis is a complication of chronic cachexia occurring as the result of some systemic disease, notably tuberculosis, syphilis, or prolonged suppuration. It is of little clinical importance.

Amyloidosis causes the kidney to enlarge and take on a waxy appearance, but structurally there is comparatively little change. Under the microscope the glomeruli will be seen to be involved in the amyloid deposits. These may be so located as to interfere with the free flow of blood through the individual glomerulus, which eventually may be converted into a shapeless mass that, when stained, will show the appearance peculiar to amyloid degeneration. There are secondary degenerative changes in the tubules.

Though degeneration is a prominent feature of this disease, it seldom occurs in pure form, and nephrosclerosis usually supervenes promptly and modifies the clinical and pathological picture.

The Nephrosis of Pregnancy. The nephrosis occurring with pregnancy is of more importance to the average practitioner than is the amyloid kidney. This, also, is rarely "pure." Nephritis of some type—acute, subacute, or chronic—will usually be observed in conjunction with it. A previous nephritis, perhaps manifested in early childhood and long forgotten, is likely to recur in the pregnant woman, and at this time a toxic nephrosis will usually be initiated in connection with the recurrent nephritis.

Chemical Nephrosis. Chemical nephrosis is also of clinical importance. This is an acute form of nephrosis due to mercuric chloride or other poisoning. The majority of cases are of suicidal origin. Death in such cases may be due to extraurinary lesions caused by the poisonous agent, or to renal failure resulting from the chemical injury to the renal parenchyma.

The kidney lesions may vary from simple cellular changes to generalized tubular necrosis with renal insufficiency or anuria. Upon the amount of poison carried to the kidneys by the arteries depends in large part the degree and distribution of the degenerative lesions. Although the extent and type of degeneration vary greatly, the lesions are largely confined to the proximal convoluted tubules, with relatively mild or no changes in the glomeruli. Usually there is some manifestation of destruction in the collecting tubules, though this may be very slight.

(3) *Sclerotic Diseases of the Kidney*

Sclerotic lesions of the kidney may be divided into two groups: (1) renal sclerosis without hypertension, (2) renal sclerosis with hypertension.

The *arteriosclerotic* kidney is a part of a generalized arteriosclerosis. Sclerosis of the renal artery and its larger branches causes infarctions; and the resultant scarring, together with areas of normal parenchyma, produces the contracted, nodular, so-called "senile" kidney. This gives no characteristic clinical picture, although impairment of function is usually slight.

The *arteriolosclerotic* kidney is the third form of Bright's disease. The essential lesions are in the blood vessels. As in the "senile" organ, the kidney is contracted and irregularly nodular, with areas of functioning parenchyma persisting between the scarred areas resulting from infarction, so that normal function is maintained. The granulations, however, are much finer than in the arteriosclerotic kidney. Hyalinization and perivascular fibrosis characterize the intima of the veins and arterioles. Obliteration of the glomeruli gradually occurs, with atrophy of the related tubules. The larger vessels are also involved. A malignant type has been described in which there is greater and more rapid destruction, with renal insufficiency. Two types of renal arteriolosclerosis can therefore be recognized: (1) renal arteriolosclerosis without renal insufficiency, with the clinical syndrome of benign hypertension; (2) renal arteriolosclerosis with renal insufficiency, or the malignant form.

(4) *Treatment of Nephritis and Nephrosis*

The treatment of the various forms of Bright's disease has always been considered a purely medical situation, except for the fairly well-established operation of decapsulation and the treatment of ureteral stricture and other obstructive lesions of the urinary tract which are regarded,

by Hunner and numerous others, as having a direct bearing upon the problem of Bright's disease.

In general, the non-surgical treatment of diffuse glomerulonephritis is directed to the establishment of conditions which will provide the ailing kidneys with as complete rest as possible and give the damaged renal tissue the greatest possible opportunity for regeneration. Renal dysfunction due to degenerative lesions of the kidney present an extremely difficult, if not insurmountable, obstacle to successful treatment by measures now at our disposal.

Diet. When blood chemistry shows high nitrogen retention, a controlled protein intake becomes absolutely essential. Therefore, dietary regulation is the physician's first concern. It is now generally conceded, however, that it is a mistake to limit the protein intake too severely for long periods. If edema is persistent, a considerable amount of protein may be passed in the urine—enough to constitute a very serious loss; and if the intake is restricted, the patient may literally be starved to death. As a result of increased protein metabolism, more urea is formed in the kidneys, as this doubtless has a certain diuretic effect upon the urinary proteins.

Cameron, from his own experience and a careful study of the evidence favoring a liberal protein intake, recommends only moderate restriction during the initial and terminal stages, with, under other circumstances, a basic ration of 70 to 80 gm. per day, to which should be added the equivalent of the protein lost in the urine.

Addis and Lew, and Bergman and Drury, in experiments with rats, arrived independently at the same conclusion, namely, that the deleterious effect of meat protein in acute glomerulonephritis is due to the high content of potassium. States McCann, commenting on the findings of these investigators:

If the foregoing observations and interpretations are correct, the amount of protein may prove to be not as important as its source. Milk proteins may be less objectionable from the standpoint of having less potassium. One may also speculate as to whether the toxic effects of potassium might not be removed if there were a proper balance of other mineral substances, such as calcium and sodium.

In cases which display much tendency toward nausea and vomiting, so that food is retained with difficulty, a Murphy drip, using 50 per cent glucose solution, provides nourishment while resting the outraged stomach, and by the high concentration of glucose gives a smaller water intake and thus lessens the strain upon the crippled kidneys. As the

glucose solution requires no digestion before it is absorbable, it will be found a valuable aid in many of these difficult cases.

In the benign forms of nephrosclerosis, it is seldom necessary to limit the protein intake. On the other hand, when the case has advanced to the malignant form, with a high percentage of urea-nitrogen present in the blood, the amount of protein ingested should be limited to the utmost. The therapist encounters the greatest difficulty when dealing with a mixed type of Bright's disease, in which both excessive blood urea and edema are prominent features. Often it is impossible to tell whether the edema is due to cardiac failure, or is solely the result of disturbed renal function, and only by continual watching and the cautious employment of whatever seems to be the best therapeutic practice at any given period of the disease can the best interests of the patient, both dietetic and otherwise, be served.

In the nephroses of children, Farr and Van Slyke have found that, when the plasma albumin concentration is above 1.2 gm. per 100 cc., edema can usually be controlled satisfactorily by simple restriction of salt, together with an adequate diet.

In lipoid nephrosis, the best results have been obtained by the use of high carbohydrate diets, blood transfusions, and diuretics.

Renal Decapsulation. Renal decapsulation is the stripping from the kidney of the greater part of its fibrous capsule. This method of treatment was first advocated for patients with Bright's disease by Harrison, in 1896. It has been widely employed in all types of Bright's disease, both acute and chronic, as well as in nephralgias and acute renal infections. Numerous hypotheses have been advanced to explain the mechanism of improvement in renal function following decapsulation, none of which is satisfactory. The operation is most frequently done in cases of acute glomerulonephritis, pregnancy toxemia, and mercuric chloride poisoning, the theory here being that if the fibrous covering is stripped off, the congestion will not be enclosed in a firm capsule and the edema of the kidney will not, therefore, result in complete dysfunction of the organ.

The indications for decapsulation in various types of nephritis and nephrosis are still indefinite, and the operation is employed more or less empirically. Though we admittedly are unable to predetermine the renal changes which decapsulation might be expected to alleviate, and though the results in the majority of patients have been unsatisfactory, the operation produces definite improvement in some cases and in others

has apparently been life-saving. It should, therefore, be considered in certain cases of anuria or oliguria occurring in the course of nephritis or nephrosis when medical measures have failed (Operative Treatment of the Kidney: Decapsulation, p. 1707).

The best results from decapsulation have been in acute glomerulonephritis, especially in children, certain cases of chronic glomerulonephritis and of chronic nephrosis with edema, and, particularly, in pregnancy toxemia. It is probably never indicated unless there is anuria or oliguria. While the results have been less satisfactory in toxic nephrosis due to mercuric chloride poisoning, decapsulation, together with the intravenous administration of large amounts of saline and glucose, still appears to be the most rational treatment for chemical nephrosis with anuria.

(5) *Uremia*

Uremia is the presence in the blood of the urinary elements normally excreted by the kidneys, and the toxic condition produced by their retention. It is a development of the chronic form of nephritis as a rule, although it may also occur in acute attacks. Of the several clinical forms of uremia, only two need be considered here: (1) the acute convulsive type and (2) the chronic retention type.

Acute Convulsive Uremia. Acute convulsive (or "eclamptic") uremia develops rapidly, and is a relatively common occurrence in the course of diffuse glomerulonephritis, both acute and chronic. The syndrome is not seen with nephrosis except when there is much edema, which has involved the face and, inferentially, the brain. Its familiar manifestations are attributed to constriction of the smaller arteries within the brain; this is but part of a generalized vascular constriction, with edema and swelling having a relationship to that seen elsewhere in the body during these attacks. Examination of the eye grounds reveals this vascular constriction in the brain clearly in the narrowing of the ocular vessels. Elwyn states that variations in the rapidity or slowness with which the edema of the brain is produced are in all probability responsible for the variations in the clinical picture.

The patient first complains of headache, which constantly increases in severity. This is followed by slight twitching in the limbs or about the face, after which the body becomes rigid, with the legs extended, the joints flexed, and the jaw tightly locked. The rigidity involves the chest muscles, and the face—at first pale—soon becomes purple, with

visible swelling of the cervical veins. The eyes are insensitive to light, the pupils dilated and rolling. The tonic stage of the convulsion lasts for from 15 to 30 seconds, after which the clonic period sets in, with convulsive twitchings of the face and limbs, or even of the entire body. The intervals between the seizures gradually lengthen, and the seizures finally cease and are followed by profound coma, with stertorous breathing similar to that in epileptic seizures. All the mental symptoms of cranial neoplasm may appear—such as confusion, mania, hallucinations, and delirium—making differential diagnosis difficult. Again, only depressive symptoms will be in evidence, the patient remaining stuporous and unresponsive to stimulation of the sensorium.

Chronic Retention Uremia. Chronic retention uremia seldom develops except after kidney function becomes seriously impaired. It usually appears as a late manifestation of chronic Bright's disease, and its clinical symptoms are indistinguishable from those induced by urinary-tract obstruction due to mechanical causes wholly unrelated to Bright's disease. Chronic retention uremia, therefore, is not pathognomonic for any renal or urinary-tract lesion, and its cause should be carefully sought in the few instances where the patient's previous medical history has not already furnished the information. Though this form of uremia may occasionally supervene when the functional ability of the kidney has not been deemed seriously lessened, as a rule it appears late in the course of chronic Bright's disease, being ushered in by headache, vertigo, loss of appetite, weight, and strength, and the clinical syndrome regularly associated with the sclerotic form of Bright's disease in particular. Hypertension increases constantly, and the urine shows many casts, much albumin, and other evidences of lessening of renal efficiency, as well as a steady decrease in the total amount excreted.

With increasing renal impairment, the patient experiences muscular contractions, cramps in various parts of the body, itching of the skin, and other subjective sensations. As the uremia becomes more profound, the digestive disturbances and bowel irregularities are accentuated: the diarrhea may eventuate in an ulcerative colitis, and sometimes an acute gastritis with ulceration appears as a terminal manifestation. The mouth is dry, the tongue heavily furred, and the gums resemble those seen in scurvy. The breath becomes extremely foul.

Hiccough is frequently very troublesome, resisting treatment. There is shortness of breath, coming in paroxysmal attacks known as renal asthma, and in advanced cases there is the Cheyne-Stokes type of breath-

ing. When coma sets in, there is air-bunger, with a hissing sound on expiration.

The effect of the uræmic condition is noticeable in the extreme irritability displayed by persons who previously were self-controlled and even-tempered. In most cases there is a gradual but steady dulling of the mental faculties, declining into coma by slow degrees. Visual disturbances almost always arise, but other sensory irregularities vary in individual cases.

The tremendous increase of the blood's non-protein nitrogen content is the most striking feature of chronic uremia. There is a gradual lowering of blood pressure, and as the pressure goes down the nitrogen content is proportionally increased. Lessening of the carbon dioxide content of the blood determines the degree of acidosis present in a given case. It is not unusual to obtain figures of 30 to 20 volumes per cent, and some have reported as low as 10 volumes per cent. The range of the figures for non-protein nitrogen is from 100 to 300 mgm. per 100 cc. of urine, and this rises upon occasion as high as 500 mgm. Concurrently with this increase in non-protein nitrogen will be found higher values for all the other nitrogenous substances making up the blood volume: uric acid often rises from a normal of 2 to 3.5 to 10 to 20 mgm.; while creatinine, normally in a proportion of 1 to 1.5 mgm. per 100 cc., rises frequently to from 5 to 40 mgm. In uremia, the amount of blood calcium declines, while the phosphorus content rises. If the phosphorus level is high, it may be taken as an indication that the fatal termination will not long be delayed. The accompanying acidosis is probably due to the kidney's loss of power to produce ammonia, and perhaps also to the general dehydration, which would make the proportion of both acid and nitrogen correspondingly greater.

Treatment of Uremia. The physician first ascertains the cause of the uremia and attempts to relieve it. In chronic retention uremia occurring as a late manifestation of Bright's disease the outlook for the patient is uniformly poor. Treatment is palliative.

Measures that have been found useful in the treatment of uremia are high colonic irrigations and infusions of normal saline, with or without glucose. The latter are particularly helpful when the patient is subject to vomiting, as is usually the case in uremia. Infusions, not exceeding 500 cc. in volume, may be given 2 or 3 times daily. When vomiting is excessive, tap water may be injected into the rectum in 250-cc. doses every 4 hours, to prevent dehydration and dilute toxins in the blood.

Fluids should be forced if the patient is able to take them. Certain drugs, such as potassium citrate, are given to stimulate the excretion of poisonous materials retained in the blood. Thyroprotein may be administered if urinary secretion is diminished, as it usually is. The patient is given 2 cc. of the drug, followed by 1 cc. every 3 hours until 5 cc. has been given.

Acute convulsive uremia is customarily handled by the administration of such medicaments as chloral hydrate or a morphine derivative, while venesection and lumbar puncture will often stop the convulsive seizures and afford temporary relief of symptoms.

The treatment of puerperal eclampsia is beyond the scope of this book.

The Renal Factor in Arterial Hypertension

Earlier Investigations. The frequent association of renal lesions and arterial hypertension is a clinical observation of many years' standing. In 1909, Janeway published a brief note on rises in blood pressure observed after the ligation of branches of the renal arteries in dogs. In 1910, Longcope and McClintock, while studying the effect of constriction upon the splanchnic arteries, observed a relationship between chronic pyelonephritis and sustained elevation of arterial pressure. Not until 1930, however, was serious attention paid to the role that disease of the kidney might be capable of playing in high blood pressure. After Goldblatt, Page, and many others had proved by animal experimentation that certain cases of so-called "essential" hypertension indisputably have their origin in pathological conditions within the kidney, Longcope re-stated his findings of a quarter-century earlier, which he was now able to buttress by an imposing array of scientific evidence.

Experimental and clinical evidence continued to accumulate. It was concluded, from certain experimental work, that arterial hypertension was probably the result of obstruction to the renal circulation. It was likewise observed that secondary hypertension was more often associated with kidney disease than with diseases of all other parts of the body combined. Glomerulonephritis, for example, is practically always associated with hypertension. So constant is this finding that when no marked rise in arterial pressure can be demonstrated in a glomerulonephritic patient, it is safe to assume that he has the kidney lesion in a very mild form.

Renal Pressor Substances and Arterial Hypertension. Goldblatt and others continued their investigations until they had shown that

there probably exists in the normal kidney a pressor substance which is greatly increased in volume when the kidney is diseased or artificially rendered ischemic. It is assumed that, in the normal processes of metabolism, this substance is discharged into the blood stream. If the renal circulation is obstructed, or otherwise impaired, the kidney is no longer able to excrete or neutralize this pressor substance. These assumptions were confirmed by observations upon human subjects of nephrectomy upon an ischemic kidney. When such a kidney was removed, the blood pressure, which had previously been high, immediately subsided to normal.

Carrying forward the idea of a pressor substance, many investigators—notably I. H. Page and his group at the Lilly Clinic—studied renin and other kidney extracts in the hope of isolating the causal agent of increased blood pressure. Eventually they discovered what they termed “renin activator,” *i.e.*, a substance (special protein) which must be present with renin to make the latter act to induce arterial hypertension. Without positive proof, it seems highly probable that renin is an enzyme acting on a substrate, which may very well be renin activator. The final conclusion has been—so far, at least—“that the pressor substance was not renin itself but a third substance formed as the result of interaction of renin and renin activator... a heat-stable, dialysable material with strong pressor properties,” which was called “angiotonin” by Helmer and Page. When administered to experimental animals, this substance is found to raise the blood pressure to a considerable degree without producing any of the severe symptoms which accompany the artificial production of hypertension by other means, such as placing a clamp on the renal artery. By the employment of established tests of renal function, it was found

... that the filtration rate (insulin clearance) is well maintained, while there is in many—but by no means all—a tendency to reduced renal blood flow. Maintenance of filtration at normal levels while plasma flow is somewhat reduced indicates that there has occurred an increased pressure head in the glomerular capillaries, so that more water is squeezed from less blood. Since, in spite of increased systemic pressure, renal blood flow is often less than normal, it is apparent that there must have occurred increased renal resistance. This increased resistance is due to constriction distributed between the afferent and efferent arterioles.

Since such constriction is characteristic of hypertension, it would be reasonable to

depend on a balance struck between increased resistance and increased pressure.

Notwithstanding these findings, Page is still doubtful whether the therapeutic use of kidney extracts will prove an efficient way of curing or benefiting arterial hypertension in human subjects. But that there is some room for activity by the renal surgeon, we have already had practical demonstration. The medical side of the problem is still in the experimental stage, and positive proof is lacking.

Current Theories of Mechanism of "Essential" Hypertension. The views of Page have been questioned by a number of investigators. At present, there are two main theories of the mechanism of "essential" hypertension: (1) that of Page and his followers, and (2) that of the European school, represented by Holtz.

To sum up Page's views: When the pulse-pressure of the kidneys is reduced, they release renin, which acts upon a so-called "pseudo-globulin" in the blood to form "angiotonin"—the pressor substance. Hypertension is the result of angiotonin's action upon the arterioles; or, possibly, the action of some secondary product of angiotonin—this is not yet clear.

Some investigators, while agreeing with Page in the main, think that renin is an enzyme which acts upon its globulin substrate to form a pressor substance which Munoz and his coworkers have called "hypertensin"—merely another name for angiotonin. This substance may then be destroyed in the blood by another enzyme, which they have dubbed "hypertensinase."

The European view is that, as the kidney contains decarboxylase and amine oxidase (which acts only in the presence of oxygen), when the oxygen supply is lessened or cut off, there is a partial interruption of the amino-acid metabolism. This metabolic disturbance brings about the production of amines, many of which are pressor substances.

Both views rest upon the fundamental concept that arterial hypertension is a state characterized by an increase of peripheral resistance, this being due to the presence of certain pressor substances in the circulating blood. If the kidneys are ischemic, they will release these pressor substances, and thus establish a vicious circle: The pressor substances bring about changes in the arterioles. Renal arteriosclerosis tends to maintain ischemia, which gives rise to arterial hypertension, which again gives rise to arteriosclerosis, and so on.

The reason for the wide variations of the conditions we are wont to group together as "essential hypertension" has been thus set forth by Schroeder, of the Rockefeller Foundation: Arterial hypertension

usually depends upon two factors (rarely one) which cause a third, a similar one, to come into being. Obviously, the rate of progress of the condition resulting from these factors is determined by the relative parts which each play. If the functional element acts alone, the course of the disease is prolonged (benign), depending for the most part upon the degree and frequency of action of the renal vaso-constrictor nerves, and those factors which influence them. Patients exhibiting symptoms predominantly of nervous origin vary, therefore, in their course from long-standing "mild" hypertension, to a severe disease characterized by a labile blood pressure easily influenced by rest and sedatives. Rarely does the course become "malignant."

If the structural element is progressive and the functional one continues to exert its influence, the course of the disease is more rapid, and death results from renal insufficiency. On the other hand, if the structural element is stationary or only slowly progressive (as in arteriosclerosis), the course depends upon the influence of the functional element. If both the functional and the structural elements act with increasingly greater influence, a "malignant" course results. . . . Other cardiovascular conditions also affect the outcome.

Treatment. From the considerations just cited, it would appear that attempts to treat renal hypertension, or any other manifestation of this underlying basic condition, must be regulated to meet the special set of circumstances appearing in each individual case. Three general classifications, however, can be made:

1. The functional or spasmodic factor can be altered if the existing conditions which are causing constriction of the blood vessels supplying the kidney can be eliminated. This might be done by

- (a) Sedative medication to lessen the effects of these stimuli.
- (b) Training of the patient so that he will ignore the stimuli and cease to react to them.
- (c) Surgical intervention upon the sympathetic nerves which control certain functions of the kidney.

2. Surgery may be employed to alter the structural (organic) factor by

- (a) Removal of an ischemic or otherwise diseased kidney.
- (b) Surgical correction of degeneration of the renal vascular system.
- (c) Operations to increase the renal blood supply, for example, decapsulation of the kidney.

3. Neutralization or destruction of the pressor extracts responsible for hypertension might be brought about by the administration of some of the extracts recently offered by investigators, the value of which is still problematical.

Medical treatment has not to date proved satisfactory, although it is still the main line of defense. The idea of neutralization of one element of the blood by the introduction of an extract of another—antagonistic—

type, while founded upon a well-recognized premise, is yet in the experimental stage, and cannot find general usefulness for some time to come. This leaves only surgery as a proved means of lessening, or, in particularly favorable cases, abolishing, arterial hypertension (see Surgical Treatment of Arterial Hypertension, p. 1710).

Urological Conditions Associated with Hypertension. It has long been known to urologists that a number of clinical conditions of the urinary tract are associated with hypertension, and that relief of the condition is commonly followed by lower blood pressure. Impairment of renal excretion may or may not accompany the hypertension, but there appears to be no particular relation between the two.

Fishberg summarizes the renal conditions that may lead to hypertension as follows: (1) polycystic disease—only when it has reached the stage of extensive destruction of the renal parenchyma, (2) chronic pyelonephritis (not during the acute stage), (3) tumors of the kidney; (4) gross occlusion of the renal artery; (5) renal hypoplasia, (6) periarteritis nodosa—only when the arterioles are implicated; (7) glomerulonephritis; (8) nephrosclerosis, (9) rarely in late amyloidosis, and after several days of anuria in mercury poisoning.

Chronic pyelonephritis, causing extensive atrophy of the renal parenchyma and sclerosis of the blood vessels, is probably the most common urological condition responsible for hypertension. In unilateral pyelonephritis, the vascular lesions, which are similar to the severe obliterative lesions found in malignant nephrosclerosis, may be confined to the affected side, and with such unilateral involvement hypertension may or may not be observed. In contrast to the vascular lesions of primary malignant hypertension, which are generalized, those of chronic hypertension due to pyelonephritis are mainly limited to the kidney. Although organic diseases of the cerebral and coronary vessels are observed in many of these cases, they occur less frequently than in hypertension of other origin. The exact relationship of chronic pyelonephritis to hypertension is not clear. It is well known that one patient with pyelonephritis may have hypertension long before there is any appreciable diminution in renal function, and another may die of uremia without having developed hypertension, while a third may develop hypertension only in the uremic stage. Renal vascular occlusive changes, rather than the gradual destruction of the renal parenchyma, have been generally considered to be the causative factor in the production of hypertension. Of primary importance to the urologist is the fact that pyelonephritis can be diagnosed and treated in

its initial stage, thus avoiding its disastrous sequelae. Also, removal of a badly damaged and atrophic kidney, when its mate is normal and functionally efficient, often results in disappearance of the hypertension.

Urinary obstruction is often associated with hypertension, and relief of the obstruction is commonly followed by lower blood pressure. Obstructions associated with hypertension are most frequently due to prostatic hypertrophy, congenital valves of the posterior urethra, and the fairly common vesical neck obstructions in children. Whether the hypertension is due to the effect of the obstruction on the kidneys, or, as is generally believed, is secondary to an associated chronic pyelonephritis, is not clear. Various combinations of urolithiasis, obstruction, and atrophic types of infection may also be responsible. Removal of the obstructing stone and drainage should produce favorable results if the hypertension is recent and there is no evidence of arterial changes elsewhere in the body. Schroeder and Steele studied "essential" hypertension in 71 young patients who showed no functional impairment of the kidneys. Intravenous pyelograms revealed unsuspected abnormalities in 50 of the 71 patients, about one-half of them some form of urinary obstruction.

Renal tumors, which interfere with the blood supply of the kidney sufficiently to produce a renal ischemia, may cause hypertension. It is well known that many children with Wilms' tumors, which usually involve the kidney by pressure atrophy, show definite hypertension.

Unilateral or bilateral *partial occlusion of the main renal artery*, resulting in ischemia of the renal substance, may cause hypertension. Such occlusion may be due to thrombi, tumor invasion, or pressure from without by tumors, anomalous vessels, ectopic kidneys, etc. If the cause of the blockage cannot be removed, and if the condition is unilateral and the other kidney sound, nephrectomy is indicated, and has been followed by relief of the hypertension.

At present, it seems probable that while, in the majority of the cases now grouped under the term "essential hypertension," the condition depends on atheromatous narrowing of the large renal arteries at or near the aorta, in a certain number of cases (variously estimated at 15 to 20 per cent) the rise in blood pressure is due to unsuspected disorders of the kidneys or urinary passages.

Disturbances of Renal Function Following "Crush" Injuries

Disturbance of renal function as an indirect result of severe trauma, usually to the limbs, when the kidney itself has suffered no visible injury,

was widely observed during the air raids suffered by the British people earlier in the present conflict. Though designated as a "new syndrome," the fact that injury to other parts of the body may impair or wholly abolish renal function has been known for a long time; but the new form of warfare against the civilian population has brought it sharply to the attention of medical investigators.

In a discussion before the Royal Society of Medicine, in December, 1941, E. G. L. Bywaters offered the following classification of the syndrome:

Impairment of Renal Function After Trauma to Distal Parts

1. *Functional azotemia* due to decreased glomerular filtration or increase in formation of waste products.

Examples: Oligemic shock, including hemorrhage.

Dehydration or electrolytic loss.

Pericardial tamponade and vascular stasis.

2. *Organic changes.*

Examples: Crushing injury, burns, some types of obstetric shock, traumatic liver necrosis, intravascular hemolysis, tubular or ureteral blockage due to sulfapyridine.

It is thus evident that the cause of such renal impairment may be various, even though its manifestations are identical.

Bywaters comments:

It was not until after the first case had been published that we discovered that this "new" syndrome, occurring in patients pinned for hours under the debris of bombed houses, was not new at all. It was recognized in Germany during the 1914-1918 war, mentioned in official books on military surgery, and worked up pathologically; indeed, it had only been missed by a week in 1909 following the Messina earthquake; there, the German relief hospital arrived on the fourteenth day and observed only the muscle and skin gangrene in recovering cases... it does occur in civil practice following mining accidents... and also... following traumatic injury to main vessels.

Clinical Picture. Most of the cases have occurred in patients who have been huried in debris, with limbs pinned down by heavy beams or fallen masonry, for a considerable period—often 12 to 18 hours. One case has been recorded, however, where rescue took place only 45 minutes after the accident. On admission to the hospital, most persons are in a state of shock, depending upon the amount of blood lost and the extent and duration of the injuries sustained. As a rule, they revive promptly in response to transfusion of blood or serum, and may appear in fairly good condition—if visible trauma is not severe—for hours or even days. But

the volume of urine passed will steadily decrease, and the blood-pressure reading will steadily rise; while blood examination will reveal retention of phosphate and potassium, as well as urea, with a decreasing alkali reserve. The usual indications of uremia soon set in, and death occurs some 7 or 8 days after the original accident, the behavior of the heart being similar to that seen in potassium poisoning.

Pathology. In those patients who died with uremic symptoms after the lapse of a week—that is, who did not succumb as the direct result of the trauma to the limbs or trunk—the kidneys, at autopsy, were markedly swollen and moist, but otherwise not abnormal to the unaided eye. But under the microscope severe damage to the distal convoluted tubules was evident, with the massing of pigment casts in the collecting tubules. The microscopic picture has been thus described by J. Shaw Dunn:

The lesion should be described as an acute tubular nephritis, while its accompanying functional disturbances of anuria or oliguria, marked loss of concentrating power, and retention of urea could readily be paralleled in mercurial nephritis of man and in experimental tubular nephritis of animals. . . . The lesion . . . was restricted to the lower segments of the nephrons: viz., the ascending limbs of Henle's loop and second convoluted tubules, whereas almost all the substances which in natural diseases or experimentally caused tubular nephritis, affected the upper segment of the first convoluted tubule. Selective damage of the lower nephron segments appear to have been little known in human disease, and few substances employed experimentally have had this effect. It might be significant, however, that two substances which have occurred naturally in human metabolism, namely, uric acid and phosphoric acid, have been shown capable of this effect. It has been suggested that the special localization of effects of these agents is due to acidification of the renal filtrate in the tubular segments concerned, and it seemed probable that the localization of the lesion in the kidneys of crush syndrome was also contributed to by acidification of the filtrate in addition to the usual factor of concentration. The presence of the brown casts of myohemoglobin in the tubules was at any rate confirmatory of the view that the renal change was caused by a positive factor derived from muscle, and carried to the kidneys in the blood stream, rather than from loss of something from the blood into the tissues.

Treatment. The mortality rate being very high, it has been difficult to evaluate treatment, or even to judge whether or not efforts directed toward the relief of the original injury have benefited or aggravated the renal condition. There is a suspicion that the patients who recovered did so in spite of, rather than because of, the remedial measures employed. Surgeons can come to no agreement as to the wisdom or necessity of amputating the injured limbs before the effect of the biochemical changes in the blood can be manifested in the kidneys. The *British Medical Journal* comments editorially:

On the therapeutic side there are as yet few clear guiding lines as to what should be done. In at least one instance fairly early amputation of the affected limb failed to save life, while in others recovery occurred without amputation. It therefore cannot be said that crushing is in itself an indication for removal of the limb. There is a case for the trial of suprarenal cortical hormone with careful biochemical control, although it should be noted that the suprarenals showed little change at necropsy. . . . Minor crushes are of great importance and necropsies should be performed on those patients who die soon after release.

Only by careful study can a basis of rational and effective treatment be reached.

Renal Rickets

Renal rickets is a form of stunted bodily development in association with, and probably resulting from, renal deficiency. The patients are children and adolescents of either sex. There is progressive renal deficiency, as evidenced by gradually diminishing phenolsulphonphthalein output and rise of nitrogenous substances in the blood, with, usually, a blood chemistry picture of lowered calcium and increased phosphorus; these are seen in conjunction with rachitic bone changes, dwarfism, and, if the patient lives to puberty, infantilism

Historical. The first clear description of this condition was that published by Lucas in 1883, although clinical reports on single cases had previously been made by Stenier and Neureutter (1870) and Goodhart (1872). Lucas called the disease "a form of late rickets associated with albuminuria." Barber, in 1911, defined it as "a condition of stunted development, associated with bone deformities of the 'late rickets' type, due to an insidious chronic interstitial nephritis of obscure etiology." Ellis and Evans found 80 cases on record up to 1933; while Howard, in 1938, stated that the number of reported cases was "still . . . under 100."

Etiology: Pathology. The cause of renal rickets is undetermined. Etiological theories that have been postulated are:

(1) Chemical deficiency due to renal insufficiency resulting from some form of chronic nephritis or congenital polycystic disease.

(2) Chemical deficiency due to renal insufficiency resulting from obstructive uropathy.

(3) Hyperparathyroidism, either primary or secondary to renal deficiency.

Earlier writers stress the apparent importance of the ordinary forms of chronic nephritis in the production of renal rickets. Most later writers, on the other hand, emphasize the frequency with which obstruc-

tive uropathy is found in conjunction with the rachitic changes, and are inclined to believe that the renal impairment is due to hydronephrosis, which, in turn, is caused by some congenital or acquired obstruction in the urinary tract. Of the 20 patients reported upon by Ellis and Evans, 14 had dilated ureters, leading these authors to conclude that the underlying lesion is a functional failure of the vesico-urethral sphincter, "either the occurrence of spasm or, as is more probable from what is found elsewhere, a failure of relaxation." Price and Davis (1937) state:

It is . . . improbable that any of the ordinary forms of diffuse or focal chronic nephritis are constantly concerned [in the etiology of renal rickets], for in the great majority of these cases there is neither an antecedent history of acute nephritis, nor any clinical or postmortem evidence of hypertension or cardiac hypertrophy. The histological picture presented by the kidneys provides still further evidence that the process is an unusual one. Advanced glomerular destruction and gross tubular dilatation supply the usual evidences of renal failure, but the occasional indications of antecedent acute or subacute toxic nephritis, as provided by thickened and adherent tufts or crescents in Bowman's capsules, are completely absent, as are also any evidences of a causative hypertensive arteriosclerosis. The only findings indicative of the possible cause of the renal destruction are suggestive of a true chronic interstitial inflammation, such as is provided by chronic pyelonephritis.

The relation between the rachitic changes and renal deficiency is obscure. It has been suggested that in renal insufficiency phosphate retention results in low serum calcium, and in an attempt to overcome this altered calcium-phosphorus equilibrium, the parathyroid glands become hypertrophied. Overactivity of the parathyroid glands brings about the bone changes, the state of the bones seen in renal rickets being identical with that characterizing primary hypertrophy of the parathyroids or following the experimental administration of parathyroid extract in animals. The hyperparathyroidism is rather a direct result of the renal insufficiency, for though the bone changes resemble those of rickets, the essential finding is osteoporosis, such as is seen in hyperparathyroidism (Lyttle).

No etiological theory as yet put forth fits all the conditions in the complicated syndrome designated as "renal rickets." We are inclined to agree with the conclusion arrived at by Price and Davis, namely, that renal rickets is really a syndrome common to two separate and distinct diseases, one of these being the late sequelae of hyperparathyroidism, and the other a definite renal deficiency, either of which may arise from any one of a number of etiological factors.

Symptoms and Diagnosis. Most of the children are thought to be

normal at birth, but by the time they reach the age of 2 years, marked evidences of retarded bodily growth are usually to be noted. In the type of rickets traceable to avitaminosis, marked skeletal deformity is not usually apparent as early as this. Inability to metabolize properly certain minerals—phosphate retention and calcium loss—can be demonstrated biochemically; but often the malfunctioning of the kidneys will not be discovered until the child has been under medical supervision for some time. This emphasizes the importance of making urological examination a part of the investigation of children's ailments, irrespective of whether or not the clinical evidence points to the urinary tract. Blood chemistry is likewise very important. It is on the blood and urinary findings that diagnosis and differentiation from the more common type of rachitic process must largely rest. Normal children have a phosphorus reading between 3.5 and 5 mgm., and a calcium reading between 9 and 11 mgm. In the more common form of rickets the blood calcium increases while the blood phosphorus decreases. In renal rickets we find the exact opposite: the blood calcium decreases and the blood phosphorus increases.

Treatment. Little can be said regarding treatment. Most of these unfortunates are beyond aid when medical help is sought. It appears probable, however, that were the obstructive uropathy dealt with early in life, the bone changes might be prevented or greatly alleviated. Though most parents state that nothing abnormal was noted during infancy and early childhood, it is likely that a careful investigation of urinary function would have shown renal deficiency long before the appearance of such manifestations as *genu valvum* or *varum*. Howard (1938) removed an obstruction at the bladder neck of a 10-year-old boy with a slight left *genu valvum*. There was regurgitation up the left ureter, and the kidneys were shown by x-ray to be much below normal size. At the time of writing, 6 years later, the boy was well and able to carry on a normal existence. This author feels confident that had he not removed the vesical-neck obstruction, the boy would not have been alive.

Dietetic measures have been tried without any noticeable success. Endocrine therapy would seem to offer promise of aid in those cases thought to have a parathyroid involvement. However, the necessity for first putting the urinary tract in as nearly normal a condition as possible would still remain paramount.

Non-Specific Infections of the Kidney and Renal Pelvis

The frequency and morbidity of renal infections demand that the problems involved in their prevention, diagnosis, and treatment be understood by all practitioners of medicine. While almost every type of pathogenic organism has been known to invade the kidney, the list of common invaders is a fairly brief one. The organisms which most frequently cause renal infections are the colon bacillus, tubercle bacillus, staphylococci, and streptococci. Clinically, the various organisms and the infections they cause are most conveniently classified as (1) specific and (2) non-specific, or pyogenic. The specific organisms include the tubercle bacillus, gonococcus, *Spirochaeta pallida*, *Bacillus typhosus*, *Schistosoma haematobium*, echinococcus, and *Actinomyces bovis*. The pyogenic organisms are of two groups: (1) bacilli and (2) cocci. Bacillary infections predominate.

Routes of Bacterial Invasion. Organisms can gain entrance to the kidney (1) from a distance, by way of the blood stream (hematogenous infection), (2) by ascension through the lumen of the ureter (urogenous infection), (3) by way of the lymph channels (lymphogenous infection), (4) from an external source, as (a) through a fistula, or (b) on an infected foreign body which has penetrated the kidney. Exact determination, clinically, of the route of invasion is seldom possible, and often neither surgical exploration nor autopsy will definitely show how the infection started.

Hematogenous Infection Most renal infections undoubtedly develop as the result of direct implantation of bacteria brought to the kidney by the blood from some distant focus. The organisms most commonly responsible are the colon bacillus and the *Staphylococcus aureus*.

Experimentation has shown that the kidney is not normally a filter of bacteria. Injury to some part of the renal unit permits the passage of the organisms, although such injury may not be discoverable clinically. Renal infections occur because the invading organisms are either very numerous or very virulent, and the resistance of the kidney has been lowered by trauma, disease, or obstruction. The capillary blood vessels of the glomeruli may be obstructed by the bacteria in the blood stream, resulting in local suppuration; or the germs may permeate the tubules and reach the medullary substance, where they set up abscesses; or the infection may begin in the renal pelvis, thence spreading upward into the kidney substance. These cortical and medullary abscesses are usually scattered and circumscribed at first, but may coalesce to form a large

abscess of the kidney. This may rupture directly into the renal pelvis, or the pus may reach the pelvis indirectly by gradually percolating through the renal tubules, or the abscess may rupture into the perinephritic fat.

The *bacteriemia* of hematogenous renal infection may have a general or a focal source. The general sources are specific infections and infectious fevers. The focal sources are infections of the skin (boils, carbuncles, etc.), infected teeth, tonsils, or sinuses, pus tubes in both the male and the female, and infections of the prostate, gall-bladder, and intestines. Coccal skin suppurations and intestinal conditions (colitis, appendicitis, diarrhea, constipation) are the most frequent focal sources of pyogenic bacteriemias responsible for renal infections. The blood-stream invasions are more commonly due to the colon bacillus than to any other organism. The coccal infections are usually much the more serious. Colon bacilleurias are often transitory, subsiding spontaneously. If, however, the organisms are unusually virulent or numerous, and there is lowered resistance of the kidney, a bacillary pyelonephritis may result.

Urogenous Infection. In urogenous infections, the lower part of the urinary tract is usually already infected. Although most authors agree that it is certainly possible for bacteria to ascend from the bladder to the kidney through the lumen of the ureter, the relative frequency of ascending infection, and the mechanism of ascent, are still subjects of considerable urological dispute. It is highly improbable that a perfectly competent ureterovesical sphincter and a normally resistant ureter would permit the upward passage of infectious organisms. Experimental and clinical observations point strongly to the probability that when organisms gain the renal pelvis through the ureter they do so by a vesico-ureteral reflux. Such refluxes up the ureter are, however, a rarity, and only occur in definite pathological conditions. Any long-standing obstruction at or below the ureterovesical orifice may be responsible for a vesico-ureteral reflux, or it may be due to neuromuscular disturbances.

That bacteria can be carried from the bladder to the renal pelvis by waves of ureteral antiperistalsis is possible, though apparently rare.

From the renal pelvis, bacteria may ascend to the parenchyma of the kidney through the lymphatics or the blood stream, or, when back pressure is present, by pyelovenous, pyelotubular, or pyelointerstitial back-flow. The organisms may travel as far as the subcapsular region or into the cortical substance, where they create small interstitial abscesses. These may break into the tubules, whence the organisms reach the

medullary substance, where they set up abscesses—presenting the same picture as in hematogenous (descending) infection. Since the pelvis is always affected in such cases, this type of inflammation is called pyelonephritis.

Lymphogenous Invasion. A second channel of ascent, which was long regarded by many as responsible for pyelonephritis, are the lymphatics. The transportation of organisms from the bladder to the kidneys by the lymphatic vessels in the periureteral sheath has been considered as established on experimental grounds by Sweet and Stewart (1914), Carson (1925, 1931), and others. There has been a tendency to believe that from the lymphatics of the ureter the organisms pass to the lymphatic vessels of the renal pelvis and thence, by continuity, to the network of intrarenal lymphatics and even to the perinephritic tissues, through the communication of lymphatics of the cortex with those of the fatty capsule of the kidney.

In view of the anatomical arrangement of the lymphatics in the ureteral wall, however, it seems highly improbable that direct extension from the bladder or other pelvic viscera to the kidney can take place through these structures. The lymphatic distribution of the ureter is distinctly segmental and not continuous.

The lymphatic relationship of the kidneys to the pelvic organs, especially the bladder, was carefully studied by D. W. MacKenzie and his co-workers a few years ago. In their experiments they used dye (india ink) to simulate bacteria. The result in every experiment was a lymphatic absorption of dye, no matter where the injection was made. In each case the dye ascended via the lymphatics running up along the aorta, never passing up the wall of the ureter nor along the periureteral lymphatics. Dye injected into the trigone, around the ureteral orifices, or about the vesical neck, passed to the lymph nodes at the bifurcation of the aorta through the lymph channels. Dye injected into the lower third of the ureter passed toward the lumbar nodes, to the main chain of lymphatics. Tying off the lower end of one ureter leading to a hydronephrotic kidney, with simultaneous injection of dye into the bladder wall around the orifice of the other ureter, resulted in the absorption of dye into the aortic chain as before, suggesting its passage thence into the venous circulation of the heart, and from there to the kidneys.

The experiments of these investigators prove that no continuous lymphatic chain follows the ureter from the bladder to the kidney, and suggest that the only method by which the lymphatic system can transmit infection from the bladder to the kidney is by way of the lymph nodes

along the aorta, from which the blood stream takes up the infection and transports it to the kidney.

Invasion from an External Source. Occasionally a kidney may be infected through a renal fistula, or by an infected foreign body which has penetrated the kidney. Infection may be carried into the renal pelvis on a catheter or other ureteral instrument.

Factors Predisposing to Bacterial Invasion. Trauma and obstruction are the chief factors predisposing to renal infection—particularly the latter. Obstruction may be due to (1) congenital abnormality, (2) mechanical causes, or (3) adynamic conditions.

(1) *Staphylococcic Focal Infections of the Renal Cortex (Staphylococcic Suppurative Nephritis: Cortical Abscess: Carbuncle)*

Infections of the renal cortex are of two types: (1) staphylococcic focal infections, and (2) infections due to organisms other than the staphylococcus. The staphylococcic focal infections are primary to the cortex, and, as a rule, are limited to the cortical and medullary substances, though they may invade the pelvis. The most common type of infection in the second group is an ascending bacillary infection, the cortical involvement being secondary to a pyelitis and the final stage in the dissemination of the infection. Although bacillary infections frequently cause multiple cortical abscesses similar to those of focal staphylococcic infection, such abscesses less often lead to suppuration in the perinephrium, and pus and organisms are regularly present in the urine. The infection spreads from the renal pelvis to the cortex through the blood stream, lymphatics, or by backflow. This second group of infections will be discussed under Pyelitis, Pyelonephritis, Pyonephrosis (p. 1461).

Etiology and Bacteriology. Pyogenic coccic infections of the renal cortex are mainly hematogenous. The renal infection is usually secondary to peripheral suppurative foci (boils, carbuncles, abscesses, felons, infected wounds) or acute infections of the upper respiratory tract. Hugh Cabot has emphasized the etiological importance of the latter as original foci.

The infection of the blood stream occurs either as a mild bacteriemia or as a severe septicemia with marked constitutional symptoms. Multiple abscesses may develop in various parts of the body—in children most often in the bones, whereas in adults they frequently occur in the kidney. Coccic infections may also follow injury to the kidney, but in such cases a bacteriemia in all probability precedes the trauma, which merely increases the kidney's vulnerability to invasion by the organisms in the

blood stream. Joyce is of the opinion that a lesion of the kidney cortex may be the sole manifestation of a systemic invasion by staphylococci, or that the renal lesion may be one of several in various tissues of the body. He himself reported an abscess of the right kidney which was associated with a similar suppurative process in the left frontal lobe of the brain. This writer is inclined to regard all cortical abscesses as a single group, secondary to an external focus, and differing only in their number, size, and degree of coalescence, as well as in the length of time they have been in existence and the manner in which they chance to be distributed. If it is proper to speak of kidney "carbuncles," he asserts, we may with equal propriety designate the lesser lesions of the same nature as "kidney boils" or "kidney pimples."

Although the *Staphylococcus aureus* is the chief causative agent, occasionally *Staphylococcus albus* and *Streptococcus pyogenes* and *hemolyticus* have been identified. Mixed infections occur. Just why the staphylococcus should be able to get a better foothold in the renal cortex than any other pyogenic organism is unknown. It has been suggested, however, that its power to break down urea and to use its split products for its maintenance and growth may explain this selective affinity.

From the primary focus in the skin, respiratory tract, or other part of the body the organisms are carried to the renal cortex by the blood stream. Considerable difference of opinion exists as to just what alterations in structure or function the kidney must undergo in order to be rendered susceptible to this particular form of infection. Bilateral infection is rare, and, the organisms being blood borne, it would seem that some accessory factor—for example, trauma—must act to influence the selection of one side over the other. One theory is that numbers of small emboli, or fragments broken off larger emboli, all loaded with organisms, are conveyed by the blood stream to the renal area. If there is obstruction to the free excretory function of any portion of the kidney, suitable conditions are then provided for the retention and propagation of the organisms, which set up multiple small foci of suppuration by progressing along the lymphatic channels that accompany the renal blood vessels. Another theory is that infected embolic fragments may be enmeshed in the branches of small arteries, where the bacteria multiply freely until, broken into minute fragments by the force of the blood current, many tiny bacterial emboli are carried into some particular area of the kidney tissue. Here, if conditions are favorable, they set up

numerous foci of infection, which may coalesce to form a large cortical abscess or carbuncle.

There is also lack of definite knowledge as to how the bacterial emboli reach the kidney. It has been suggested that they either traverse an open foramen ovale and thus reach the left side of the heart, or they traverse the pulmonary circuit.

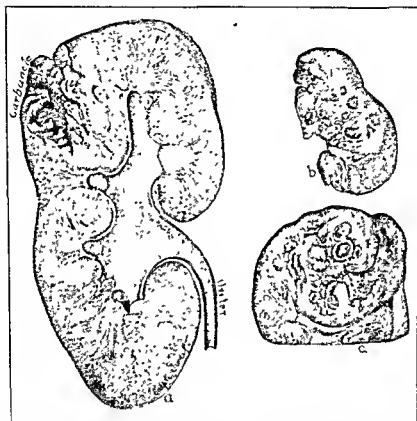


FIG. 312. Carbuncle of the kidney. Gross specimen. (a) Sectional view showing carbuncle in the upper pole (b) Appearance of carbuncle from outside of upper pole. (c) Carbuncle viewed from above. (Mathé.)

Pathology. Pus-producing cocci, in general, are productive of multiple minute abscesses in the cortical substance. These tend to coalesce, with the production of a massive abscess or carbuncle, and usually show early and marked perinephritis, often developing into a perinephritic abscess. In extreme cases there may be multiple abscesses of large and small size which honeycomb the entire kidney.

If, on its arrival within the renal vascular system, a bacterial embolus lodges in one of the glomerular vessels or in a terminal branch of a sub-

capsular artery, a single abscess, or several small abscesses, are likely to develop in this area. If the embolus lodges at the bifurcation of an artery below the cortex, definite infarction will develop; this results in multiple closely associated small abscesses, presenting the typical picture of a carbuncle, as originally described by Israel in 1905.

The renal carbuncle, therefore, is made up of multiple small foci of suppuration, and is sharply demarcated from the healthy kidney tissue by a zone of inflammation. Strands of connective tissue may separate some of the foci, but even when such formations are to be seen near the periphery, the center of the carbuncle will be found to be soft and necrotic, this "core" being actually the coalescence of numerous small pus collections so merged as to be impossible of individual recognition. It is possible that many of the conditions seen at operation, and diagnosed as cortical abscess, septic infarct, etc., are the end-stages of carbuncles whose multiple small suppurative foci have fused into single large areas of suppuration. Fewer than 100 cases of renal carbuncle have been recorded (72 up to 1935, Graves and Parkins; 88 up to 1933, Leo Brady). In our own series of several thousand kidney cases there have been only 2 cases of renal carbuncle.

Both types of infection—the multiple abscesses and the single large abscess or carbuncle—are progressive and usually lead to involvement of the perinephric fat. Occasionally a cortical abscess may rupture into a calyx or the renal pelvis and drain off satisfactorily, with the disappearance of symptoms. In the less fortunate cases, the abscess ruptures into the perinephrium, causing a perinephritic abscess. Such abscesses are a frequent sequence of both coccal infections and the cortical abscesses of ascending bacillary infection. Beer emphasized the confusion that has been caused in the interpretation of this pathological process and the origin of perinephritic abscess by virtue of the fact that at operation, in advanced cases of perinephric suppuration, one may not recognize any evidence of renal involvement. The cortical abscess, having ruptured and drained into the perinephric space, heals quickly, and the cavity in the cortex fills in with granulation tissue, so that the original abscess cavity is not recognizable to the palpating finger.

Of clinical importance are the following four types (or stages) of staphylococcal infection of the renal cortex: (1) diffuse staphylococcal nephritis, without abscess-formation, varying from a mild form that usually subsides without treatment to a fulminating type in which there is diffuse inflammation of the entire kidney, which is swollen, soft, and discolored; (2) multiple staphylococcal cortical abscesses, which may be

small and scattered, or grouped and of varying sizes, and which are commonly associated with perinephritic inflammation and abscess; (3) the large, solitary cortical abscess; (4) renal carbuncle, which is formed by coalescence of multiple small abscesses.

Symptoms. The clinical picture in coccal infections of the renal cortex may differ widely, depending upon the virulence of the organism, the patient's ability to combat the invader, and the progress of the disease. The infection may vary from an acute fulminating process to that of a subacute or chronic septic condition which may be very difficult to diagnose. There may be a considerable period of latency before the development of cortical abscesses, carbuncle, or perinephritic abscess produces symptoms referable to the kidney region.

In acute coccal suppurations, the symptoms will be those of an acute infection: high fever, leukocytosis, prostration, and septic chills. Urinary symptoms are usually absent. Acute infections have frequently been mistaken, at their inception, for a general infection such as influenza or typhoid fever, or for acute Pott's disease, respiratory disease, or, if the abscess is on the anterior surface, an intra-abdominal inflammation (appendicitis, cholecystitis, etc.). Symptoms referable to the kidney region may occur only with extension to the perirenal tissues. In most cases, however, acute lumbar pain at the onset directs attention to the kidney. There is regularly costomuscular tenderness.

Occasionally, the acute onset may rapidly progress to a toxemia which may result in death. More often the infection, if untreated, becomes chronic and recurrent, with acute exacerbations. In chronic and subacute infections, the clinical picture is less stormy, and months often elapse before the correct diagnosis is made. There will be intermittent fever, malaise, chilliness, gradual loss of weight, and progressive anemia.

There is always some lumbar pain, but this may be much less than the severity of the condition would seem likely to produce. Palpation over the affected kidney regularly reveals tenderness and occasionally enlargement of the kidney. Renal carbuncle usually gives more resistance and fixation on palpation than is the case when small multiple abscesses are present.

The severity of the symptoms in the chronic or prolonged acute cases varies with the progress of the disease. Symptoms may be marked while the suppurative focus is confined to the cortex, due to tension caused by the fibrous capsule, but may temporarily subside as the abscess ruptures into the perinephric fat. With the formation of a perinephritic abscess, the symptoms again increase, but temporarily abate as the abscess breaks

through Gerota's capsule into the paranephric space and pus ruptures downward toward the pelvis.

Diagnosis. Many cases of coccic infection of the renal cortex undoubtedly go unrecognized because of their mildness and prompt spontaneous healing.

Clinical recognition of these lesions, particularly the chronic and subacute cases, may be very difficult. In many cases the clinical picture is rather typical and therefore fairly easily recognized. In other cases, the obscure picture may delay recognition of the disease for weeks or months. Often, definite diagnosis has been made only at operation or at autopsy. This clinical confusion is due partly to the absence of urinary symptoms, the negative findings of urinalysis, ureteral catheterization, and cystoscopy as compared to the definite findings in the more common renal infections, and to the frequent presence of referred signs pointing to pleuritic or abdominal involvement.

While it may be clinically difficult, if not impossible, with the methods at present available, to distinguish between carbuncle of the kidney, solitary renal abscess, multiple cortical abscesses, suppurative nephritis, or even perinephritic abscess, one should be able to locate the process within the renal fossa.

Renal carbuncle and other coccic cortical infections are more common in men than in women (about 2 to 1). Cases of renal carbuncle have been reported in infants and children, but most of these patients are between the ages of 25 and 45 years. The right kidney seems to be affected slightly more often than the left. Bilateral involvement is rare.

A history of superficial pyogenic infection, or infection of the upper respiratory tract in the not too remote past, in conjunction with fever, leukocytosis, lumbar pain, clear urine, and physical signs such as tenderness over the kidney, with muscular defense on palpation and, sometimes, limitation of mobility, is strong presumptive evidence of cortical abscess or carbuncle. In 42 of the 67 cases of renal carbuncle reviewed by Graves and Parkins a history of previous pyogenic infection was elicited.

The value of roentgenography in the diagnosis of these cases is generally underestimated. In perinephritic abscess, or in cortical abscess or carbuncle with associated edema in the perinephritic fat, the ordinary flat x-ray plate will show obliteration of the psoas muscle, with curvature of the spine away from the painful kidney. These findings, in association with macroscopically clear urine and an unobstructed kidney, are indica-

tive of perinephritic abscess or cortical suppuration with edema of the perinephrium.

Excretory urography and retrograde pyelography have frequently been of help in the diagnosis of massive abscess and carbuncle, even before there has been perinephric involvement. The pyelogram in a fair percentage of cases will reveal deformities of the calyces, with or without changes in the contour of the pelvis. These calyceal deformities are similar to those of other compressing processes, such as cysts, neoplasms, or polycystic degeneration.

Cystoscopy and ureteral catheterization are mainly useful in demonstrating that the kidney is secreting clear urine and is not blocked. This is important, as an infected hydronephrosis may also cause curvature of the spinal column and obliteration of the shadow of the psoas muscle.

It is important to differentiate the minor cortical infections caused by pus-producing cocci from infections due to bacilli, such as *B. coli*, *B. pyocyaneus*, *B. proteus*, etc. Coccic cortical infections seldom involve the renal pelvis and therefore are not likely to be associated with pyuria unless the suppurative process ruptures into the tubules. As a rule the urine is macroscopically clear. Microscopically, it may show a few red and white blood cells. In bacillary infections, on the other hand, there is regularly pyuria, and microscopically the turbid urine discloses many clumped pus cells. The urine in coccal infections may show cocci in culture or smear, but frequently no organisms can be demonstrated. In the bacillary type of cortical suppuration, the various forms of bacilli are readily demonstrated in the sterilely obtained urine. Coccic and bacillary infections may coexist, making diagnosis very difficult.

In a considerable percentage of coccal infections the blood cultures may be positive at some times and sterile at others.

Prognosis. Any suppurative process in the kidney is a serious matter, presenting a direct threat to urinary-tract integrity and to life. If diagnosed early, however, most cortical suppurations respond well to conservative treatment. In very extensive infections, nephrectomy is indicated, and, if there has not been too much delay, the patient's chances of recovery are good. In coccic abscesses of the kidney that are part of a general, overwhelming sepsis the prognosis is poor.

The most urgent consideration in the problem of cortical suppurations is more prompt recognition of these often obscure lesions, so that proper treatment may be administered earlier.

Treatment. Many patients with the milder, diffuse types of-staphylococcic nephritis recover with no other treatment than rest in bed. Rarely, an acute fulminating infection requires immediate nephrectomy to save the patient's life. Between these two extremes is the large group of cases of multiple cortical abscesses, massive abscess, and carbuncle, frequently associated with perinephritic abscess, which almost invariably require surgery. In these cases, prompt surgical treatment offers the best—in most cases the only—chance of cure. Though a cortical suppuration may resolve or drain into the renal pelvis, with disappearance of the symptoms, this is not the usual course. Theoretically, in the milder types of cortical abscess, a short period of expectant treatment—rest in bed, with supportive measures and, perhaps, an appropriate staphylococcic vaccine—might be justified. Actually, however, the urologist and surgeon rarely see these infections until the suppurative process has reached a stage where delay is dangerous, and exploration, with nephrectomy or incision and drainage, is the only resource.

If the disease is acute and prostrating, or if the symptoms have been evident for some time and the patient is growing worse, and the presumptive evidence points to staphylococcic infection of the kidney, exploratory operation should be done.

Nephrectomy is indicated if the suppurative process is diffuse and involves all or most of the kidney, or if the patient's general condition is poor. It is also indicated when multiple carbuncles or many abscesses are present.

If the abscesses are small and limited in number, decapsulation, with puncture and drainage of the abscesses, is usually curative. In well-localized massive abscess or carbuncle, decapsulation and thorough drainage are often satisfactory (*Incision and Drainage of Renal Abscess*, p. 1686). It is sometimes possible, in well-circumscribed carbuncles, to enucleate the suppurative infarct with the finger or a blunt instrument, and pack the opening after removal of the infected wedge of renal tissue. Conditions favorable for this procedure are found infrequently, however, and as a rule incision and drainage, or nephrectomy, is necessary.

In cases of large perinephritic abscess, simple incision and drainage of the abscess should be done (*Perinephritic Abscess*, p. 1689). Many patients will recover, since the renal suppuration has already drained into the perinephric space; but if this does not effect a cure, nephrectomy may be done later. Nephrectomy in the presence of a perinephritic abscess is too dangerous to be undertaken except under most unusual circumstances.

In the past, removal of the kidney has been the usual procedure in carbuncle and other coccic infections of the renal cortex. There is, however, a growing tendency to conserve the kidney whenever possible, which has led many operators to content themselves with decapsulation and incision, trusting to thorough drainage and perhaps the use of bacteriophage or polyvalent serum to effect a cure. In some cases secondary nephrectomy is necessary, but as a rule conservative surgery is satisfactory, if done early and if the suppuration is not too extensive. Supportive measures during the drainage period are of great importance, for in many of the fatal cases the cause of death was not the local condition but the depleted systemic state, which prevented recovery from the profound toxemia even when the source of the intoxication had been removed.

(2) *Pyelitis: Pyelonephritis: Pyonephrosis*

Under the above heading will be considered all pyogenic forms of renal infection which are neither staphylococcic focal infections of the cortex nor specific types of nephritis. The pyelonephritis of pregnancy is discussed separately. The renal infections of infancy and childhood present no special peculiarities, except their much greater incidence in female children, and will be considered with those of adults.

Definitions. The terms "pyelitis," "pyelonephritis," "infected hydronephrosis," and "pyonephrosis" are used to designate various overlapping stages of renal infection, from a simple involvement of the pelvic mucosa to a functionless pus-filled sac. Almost invariably these kidneys show more or less inflammation of both the pelvis and parenchyma, and there are frequently small abscess cavities in the renal substance.

Pyelitis, or inflammation of the pelvis, is seldom an isolated condition. As a rule the infection either comes from above, in which case there is involvement of both the parenchyma and the pelvis, or is primary in the pelvis and spreads into the kidney. In either event, the resultant condition is a pyelonephritis rather than a pyelitis. The two terms are employed interchangeably by many writers—"pyelitis" referring, usually, to inflammation originating in the pelvis and chiefly affecting the adjacent portion of the parenchyma. Differentiation between pure nephritis, pyelitis, and pyelonephritis is very difficult.

Pyelonephritis is an infection of the pelvis and parenchyma. The infection may originate in the parenchyma and spread to the pelvis by way of the tubules, or it may arise in the pelvis and thence ascend to the

kidney. Pyelonephritis in its various forms is one of the more common diseases that the urologist is called upon to treat.

In *infected hydronephrosis* there is hydronephrotic atrophy combined with infection. In early cases the picture is that of a diffuse pyelonephritis, with dilatation of the pelvis and calyces. Later, secondary

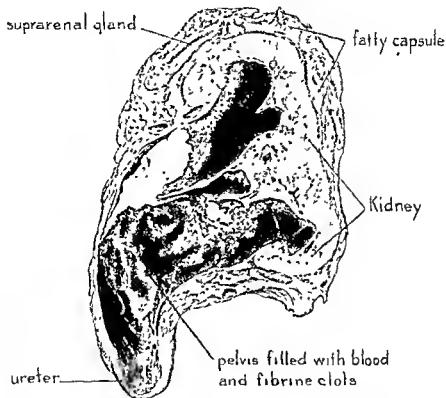


FIG. 313. Gross section of the kidney of a patient with hemorrhagic pyelitis. (Christeller.)

pressure atrophy may result in cessation of excretory activity. Still later, with shrinkage, a pyonephrosis may form.

Pyonephrosis is a purulent inflammation of the kidney, with pouching and dilatation. It is essentially the terminal stage of a chronic process, such as an infected hydronephrosis or a chronic pyelonephritis. The pus is usually more or less diluted with retained urine. In late stages

the kidney is converted into a functionless, pus-filled sac, and there are marked perirenal and ureteropelvic changes.* The kidney is already destroyed, but causes symptoms requiring surgery.

Etiology. The various ways in which infection may reach the kidney have already been considered (*Routes of Bacterial Invasion*, p. 1450). Although for many years it was believed that most renal infections ascended from the bladder through the ureter to the renal pelvis, and thence to the kidney, it now seems probable that the great majority of bacillary infections, like the coccic infections described above, are hematogenous and develop as the result of direct implantation of bacteria by the blood stream in some portion of the kidney. It should be emphasized, however, that the exact manner in which infection is conveyed to the kidney is unknown. The difficulty is that the pathologist never sees the early stages of renal infection, at which time it might be possible to make observations tending to clear up the uncertainties regarding the etiology of pyelonephritis.

From the clinical standpoint, pyelonephritis may be classified as (1) pure focal pyelonephritis without accessory urogenital abnormality, and (2) pyelonephritis with obstruction—the common form of renal infection. The source in the first group is a focus of infection elsewhere (tonsils, teeth, skin, or—very frequently—the intestinal tract), and the route is hematogenous. Focal staphylococcic infections, which are confined chiefly to the cortex and are usually unilateral, have already been considered. The infections referred to here are regularly bilateral, involve both the kidney and renal pelvis, and are due chiefly to bacilli—particularly those of the colon group. Many of the obstructive renal infections have similar foci of infection and are also blood-borne, but they are distinguished from the first group by having some accessory abnormality of the urogenital tract which causes obstruction or stasis.

In children, acute renal infections not infrequently complicate such infections as otitis media, tonsillitis, or sinusitis; or they may occur in the course of an infectious fever. Chronic infections are usually of the obstructive type and are probably chiefly hematogenous. The obstruction is usually due to some form of congenital anomaly.

Bacteriology. Any pus-producing organism may be found on culture of the urine, but the colon bacillus is identified in the majority of renal infections. Urea-splitting organisms are, fortunately, much less common. In the excellent tabulation contained in Necker's *Handbuch der Urologie* (1928), which is based on a large series of cases, colon bacilli

make up 74 per cent of the organisms found, with staphylococci second in frequency (17 per cent), and streptococci third (4 per cent)—leaving only 5 per cent of organisms of all other classes. At a large American clinic the figures published in 1938 on 200 cases ran: colon bacillus 55 per cent, staphylococci 14 per cent, streptococci 4 per cent, *Bacillus proteus*, 3 per cent—while the remaining 24 per cent covered a wide range, with only 1 or 2 cases of each type.

In chronic pyelonephritis, especially, it is important to centrifuge the urine carefully and make complete examination of the sediment, as otherwise the causative organism, or organisms, may not be identified. Mixed infections are common, and it is important that the various organisms be recognized and appropriate measures taken to get rid of all of them. In some cases of mixed infection the disease is apparently dependent upon only one type of bacteria, the others being of little or no clinical importance; while in other cases the infection refuses to clear up until every type of infective organism has been eliminated. Although colon bacilli predominate in most cases, other bacteria frequently are observed, or there may be complete absence of organisms. *Bacillus aerogenes* and *B. proteus*, as a rule, cause a greater degree of infection than the colon bacillus, but otherwise the pathological changes resulting from the presence of various types of bacteria are, on the whole, similar.

Predisposing Factors. Obstruction, stasis, and dysfunction are the most common predisposing causes of renal infection. The obstruction may be mechanical or adynamic. The result of such obstruction may be a simple pyelitis or pyelonephritis, a suppurative pyelonephritis, atrophic pyelonephritis, or pyonephrosis. If the infection is fairly mild, removal of the obstruction will frequently result in cure. In advanced cases, the infectious process may continue on to complete destruction of the kidney even after the cause of obstruction (stone, enlarged prostate, etc.) has been removed.

The most common accessory factors in obstructive renal infections are: urethrovesical abnormality (posterior urethral valves, contracture of the vesical neck, median bar, hypertrophied prostate, stricture); neuromuscular vesical dysfunction (cord bladder, atonic bladder); ureteral abnormality (ureterocele, stricture, kink, duplication, neuromuscular defects); malformation or displacement of the kidneys; hydronephrosis due to aberrant vessels and bands or to ureteropelvic obstruction; urinary stone; and pregnancy. Common predisposing factors in the renal infections of infancy and childhood are congenital abnormalities and

neuromuscular dysfunction of the bladder, particularly that due to spina bifida occulta.

Sex and Age Incidence. Renal infections are common in both sexes, but, with the exception of the coccic cortical infections described above, there appears to be a definite preponderance of female over male cases. This is due in part to the relative frequency of pyelitis and pyelonephritis in association with pregnancy, as well as to the much greater incidence of renal infections in female infants and children. All ages are affected.

Pathology. *Focal pyelonephritis without obstruction* (descending infection) is hematogenous and at first involves only the renal parenchyma. In staphylococcic infections, as previously noted, the involvement is mainly cortical, but if the infection is due to the colon bacillus or some other organism, the parenchymal infection is likely to be mainly tubular and to spread rapidly to the renal pelvis. The condition is bilateral.

Obstructive pyelonephritis (ascending infection) is probably also hematogenous as a rule. There is usually an initial simple pyelitis, the lesion thence spreading upward into the parenchyma along the renal blood vessels, producing eventually an extensive thrombosis of the peripelvic venous system (Cahot; R. L. J. Kennedy). Kennedy, in his animal experiments, found this venous thrombosis with great regularity, and feels certain that it plays an important part not only in the production of the later stages of pyelonephritis in man, such as are seen at operation or autopsy, but in the whole course of the disease, of which we can only judge from clinical observation. Upward extension also takes place by pyelovenous, pyelotubular, or pyelointerstitial backflow.

The pathological picture of the descending and ascending forms of pyelonephritis will be indistinguishable. In both forms the infection may be acute or chronic. The pelvis and calyces are often dilated. The inflammatory changes in the pelvic mucosa and wall may be catarrhal, hemorrhagic, suppurative, ulcerative, or diphtheritic. Pyelitis cystica, pyelitis granulosa, pyelitis emphysematosa, and leukoplakia may occur, though they are rarely recognized clinically. In the parenchyma, the bacillary infections frequently form multiple abscesses similar to the metastatic cortical abscesses produced by staphylococci. Microscopically, these are seen to be situated in the stroma between the tubules and glomeruli, as well as between the tubules in the pyramids. If trauma has been a predisposing factor—as, for example, when the tissues have been injured by a rough calculus—the suppurative area may be confined to the injured portion, resulting in a solitary abscess. Coccic and bacil-

lary infections not infrequently coexist, or they may appear one after another, so that, as the original invaders lose their virulence, secondary ones take their places and continue the infected state of the kidney. A pathologist, examining the later lesions, however, would probably be unable to recognize the original infection.

Both the pure focal and the ascending forms of pyelonephritis, if untreated, may progress into atrophic pyelonephritis or pyonephrosis, according to the degree and nature of the destruction.

In *atrophic pyelonephritis* the kidney is contracted to a third or fourth of its normal size, and its capsule and the perinephric tissues are thickened and adherent. The pelvis is also thickened and the upper ureter often partly stenosed. The atrophy may be diffuse or circumscribed, in the latter case resembling an infarct. Atrophic pyelonephritis may follow acute infection, but is usually a sequence of long-standing chronic infection with multiple abscesses. It must be differentiated from hypoplastic kidney, sclerotic kidney, and primary atrophy.

The more common occurrence is progressive suppuration. The term *pyonephrosis* usually suggests the thin-walled, pus-filled sac, with its dilated, flabby ureter and strictured ureteropelvic junction, so often revealed by operation or autopsy upon subjects of renal disease. There is a less typical form of pyonephrosis, however, in which the kidney will be found surrounded by a thick envelop of fatty, fibrous tissue, the organ itself being shrunken, hardened, and misshapen, and its ureter reduced to a fibrous cord—the entire pathological picture resembling that seen in certain cases of renal tuberculosis. There is also an intermediate type, in which the walls of the renal pelvis and the parenchyma of the kidney proper are greatly hypertrophied and indurated as a result of a preceding inflammatory process, while obstructive dilatation will have caused both the pelvis and the kidney proper to be dilated far beyond their normal dimensions. Hardly a trace of normal renal substance can be found, active abscesses or cicatrization due to previously active suppuration having completely replaced it. In place of the normal calyces there may be multiple cavities, the remains of the calyceal walls showing as distorted ridges of sclerosed tissue, or they may be entirely lost to view in the mass of necrotic tissue.

Symptoms. *Acute* pyelonephritis (usually referred to as pyelitis) is generally of sudden onset, often starting with fever, chills, and disturbances of urination (frequency, dysuria, urgency, pyuria), and accompanied, as a rule, by loin pain or discomfort and nausea and vomiting.

Leukocytosis is the rule. The urine is turbid, and microscopic examination almost constantly reveals pus, blood, and organisms—usually some form of bacilli, particularly the colon bacillus. The urinary findings differentiate the infection at once from staphylococcic cortical infections, in which the urine is generally absolutely clear.

The acute symptoms usually subside in from 5 to 14 days, but a bacilluria and a mild intermittent pyuria frequently persist. The case then becomes a subacute or chronic pyelonephritis.

Chronic pyelonephritis includes cases of recurring attacks of acute pyelonephritis, acute cases which have failed to clear up, and occasional cases which persistently show pus and organisms in the urine although no history of acute attacks can be elicited. There are recurrent attacks of fever, chilliness, and malaise, with accompanying exacerbations of the urinary symptoms. Leukocytosis is usually not present except at the height of the exacerbations. The most prominent symptoms being referable to the bladder, these patients frequently are treated for cystitis, when the pathology is primarily renal and treatment should be directed to the kidney infection.

The most conspicuous symptoms of *pyonephrosis* are constant or intermittent pyuria and pain or a sensation of heaviness in the affected side, usually at the costovertebral angle. The fact that many pyonephrotic kidneys come under observation only in an advanced stage of the disease would seem to argue that the symptoms are by no means always indicative of the seriousness of the condition. While all patients give a more or less definite history of "kidney trouble"—often of very long standing—many have been leading relatively normal, active lives until an acute exacerbation sends them to the physician. Sometimes the fact of the urine being loaded with pus will only be discovered when the patient is rejected for life insurance, or urinalysis is undertaken for some other reason. Again, the infection may be communicated to the perirenal tissues, setting up perinephritic abscess, for which the surgeon's services are sought, and the renal condition uncovered.

The acute attacks are characterized by pain in the lumbar region, chills and fever, sometimes painful cystitis, and a high leukocyte count. If perinephritic abscess supervenes, the symptoms will be those of acute perirenal suppuration. The patient who has no rise of temperature when seen between these acute exacerbations will manifest symptoms of bacterial toxemia, but usually only to a limited extent. There will be pus and, possibly, red blood cells in the urine, more or less extensive cystitis,

and, usually, pain and tenderness in the renal area. According to the extent of the intoxication generated by the pyonephrotic mass, there will be complaints of headache, loss of weight, lassitude and general malaise, and, in certain instances, a long train of gastrointestinal manifestations.

Diagnosis. The accurate diagnosis of all renal infections except the very acute is possible only after a complete urological investigation. Important points to be determined are: (1) whether the infection is coccic or bacillary; (2) whether it is acute or chronic; (3) whether it is unilateral or bilateral; (4) the primary focus of infection; (5) the existence and nature of accessory urogenital abnormalities causing obstruction or stasis; (6) the degree of destruction and functional impairment; (7) the condition of the opposite kidney.

The diagnosis is based on: (1) the history, (2) physical examination, (3) examination of the urine, (4) cystoscopy and ureteral catheterization, examination of separate specimens, and determination of separate function, and (5) roentgenography.

A history of fever, chills, backache, abdominal pain, and urinary disturbances, with leukocytosis, costovertebral tenderness on palpation, and turbid urine is suggestive of an acute attack of renal infection. Instrumental examination is contraindicated in the very acute stage. However, by examining the urine bacteriologically and by smear, obtaining its pH, and correlating these laboratory findings with the clinical findings, the clinician will often be enabled to arrive at an accurate diagnosis.

Examination of the urine by smear and culture should be the initial step in diagnosis. Early marked changes in the urine distinguish bacillary pyelonephritis from the focal staphylococcic infections of the renal cortex—a diagnostic factor of great importance since in both types of infection the most prominent symptoms of the acute stage, namely, the systemic symptoms, are frequently very similar, although acute bacillary infections are generally less prostrating than staphylococcic disease. In pyelitis and pyelonephritis the urine is turbid, and sterilely obtained specimens will, on bacteriological examination and staining, show pus, blood, and organisms; in focal staphylococcic infection of the cortex the urine is generally perfectly clear.

The diagnosis of chronic renal infection requires a complete urological examination. Thorough investigation must be made to determine the underlying cause of the persistent infection. The commonest single factor is obstruction to urinary drainage. This may occur anywhere in

the urinary tract, from the kidney to the external urethral meatus. Cystoscopy, functional tests, and pyelography usually give characteristic evidence of a chronic renal infection. If an obstruction to urinary drainage is found, the extent and nature of the damage from back pressure must be determined, as well as the damage from infection.

If pus and *Bacilli coli* or other organisms are present in the urine from both kidneys, but there is no urogenital abnormality, little or no tenderness in the loin (except in acute attacks), no disturbance of renal function, and the pyelo-ureterograms are either normal or show characteristic deformity of the upper ureters, without much change in the pelves and calyces (Braasch), it may reasonably be inferred that the infection is a bilateral focal pyelonephritis without obstruction. The urinary findings will differentiate such an infection from focal staphylococcic disease of the cortex, but its differentiation from the ascending type of pyelonephritis is dependent upon complete urological examination.

In all renal infections it is essential that a search be made for foci of infection in the respiratory tract, skin, genitalia, and—particularly—the intestinal tract, since the elimination of such foci is an important factor in the clearing up of chronic infection of the kidney.

The bladder findings do not, as a rule, aid materially in the identification of pyelonephritis, for often there is little or no variation from the normal cystoscopic picture. There may, however, be evidence of inflammation about the orifice of the affected kidney's ureter. In pyonephrotic kidney, the ureteral orifice may be inflamed, or it may appear to be normal but a catheter inserted into it will be stopped at the ureteropelvic junction, or before, and no urine will be obtained from that side because the kidney has ceased to function. Sometimes a worm-like string of pus can be expressed from the ureter. Such a ureter may be closed entirely at one examination but found open and emitting a stream of pus at another. This is the cause of "intermittent pyuria."

Roentgenography. Without the clinical and laboratory data the roentgenographic findings in pyelonephritis would have little value, but, when correlated with other diagnostic information, the results of pyelographic study are often of material aid in arriving at a diagnosis. Retrograde or excretory pyelography is essential for the identification of obstructive lesions or anomalies so frequently responsible for the production and maintenance of renal infection in infants and children, as well as in adults.

Ectasis of the upper third of the ureter, with little change in the pelvis

and calyces, is regarded by Braasch as characteristic of pyelonephritis. This upper ureterectasis is due in part to interference with the normal peristalsis of the ureter and pelvis because of inflammation, and in part to transitory edematous obstruction of the lower ureter. In pyelonephritis, excretory urography rarely permits adequate visualization of the character and extent of the deformity wrought by the infection. The characteristic ectasis and blunting of the minor calyces may be so slight as to be indiscernible even to the most expert interpretation. The extent of both the calyceal and the ureteral deformities are better determined by retrograde pyelography—particularly in the presence of retention, when the pelvic outline is usually well visualized.

In advanced stages of renal infection, such as atrophic pyelonephritis and pyonephrosis, roentgenography is diagnostically helpful. In atrophic pyelonephritis, the plain x-ray film will show a small kidney shadow, and pyelography will reveal irregular constricted areas in the ureter alternating with dilatation, a shrunken pelvis, narrowing and elongation of the major calyces, and irregularity and decreased size of the minor calyces.

The distorted outline seen in the pyelogram of chronic pyonephrosis is caused by dilatation of the pelvis and calyces, the eroding effects of ulceration, and distortion due to the shrinkage of scar tissue. In advanced cases, there may be no normal tissue remaining—only a great central cavity filled with the debris of the ulcerative and necrotic processes, this partly filled cavity showing in the pyelogram as an irregularly outlined, dimly defined mass which has sometimes been mistaken for a cyst or tumor. Plain roentgenograms are sometimes useful in indicating areas of calcification and distortion of the renal shadow, which may be suggestive. Since the kidney is usually functionless, or its function materially reduced, excretory urography is seldom of value except to confirm the presence of a non-functioning organ.

Prognosis. The prognosis depends on the type and virulence of the infecting organism and the early recognition and elimination of foci of infection and obstructive complications in the urinary tract. Simple pyelitis and the milder types of pyelonephritis with obstruction frequently heal without impairment of function upon the establishment of good drainage from the kidney. In other cases, temporary improvement is obtained by appropriate treatment, but recurrences are frequent, so that the urologist cannot be too confident of securing a permanent cure. The fulminating types of pyelonephritis frequently lead to suppurative

pyelonephritis, multiple cortical abscesses, atrophic pyelonephritis, or pyonephrosis. If unilateral, these generally require nephrectomy; if bilateral, they are usually fatal.

Renal infections occurring at the height of infectious fevers usually clear up promptly with improvement in the primary condition unless an obstructive condition is present, when the infection is likely to become chronic or progressive.

Treatment. The treatment of renal infections has undergone a radical change in recent years. Formerly, all treatment was more or less empiric; symptoms were dealt with as they appeared, in the *hope* that eventually the cause might be eliminated. Today, search is first made for the cause, and, if this can be determined, treatment is directed primarily toward its elimination, in the belief that if the infection is not too far advanced removal of the cause will be followed by abolition of the symptoms.

The treatment of renal infections is dependent upon (1) whether the infection is acute or chronic, (2) the type of invading organism, (3) the presence or absence of obstructive or other accessory factors, (4) the extent of destruction and functional impairment.

Acute Infections. In acute infections the use of instruments is contraindicated as a rule. The patient should be put to bed and placed on a régime of forced fluids and alkalis in the form of potassium citrate or one of the alkaline mineral waters (p. 1006). The original focus of many of these infections is in the intestines, and relief of stasis of the bowel by dietetic and mechanical means is essential. When relief of the acute symptoms has been secured, urinary antiseptics may be administered—the type of antiseptic depending upon the nature of the invading organism (see p. 1162).

In certain cases, with considerable loin discomfort or pain, when the presumptive evidence indicates obstruction (for example, the obstruction caused by the pressure of the gravid uterus in the pyelonephritis of pregnancy), it may be necessary to pass a ureteral catheter to permit better drainage. Prompt ureteral catheter drainage in these cases will not only shorten the duration of the infection, but will reduce the renal damage to a minimum.

The patient should be kept under observation until entirely relieved of symptoms and the urine is sterile and free of pus.

Chronic Infections. Chronic pyelonephritis often persists because of associated pathological conditions and anomalies of the urinary system.

The most important single factor in the treatment of these cases is the removal of any obstruction, stasis, or other accessory factor. With the removal of the obstruction, and the establishment of adequate drainage, many renal infections clear up promptly. On the other hand, failure to eliminate the obstructive factor in the kidney, ureter, bladder, or urethra will render ineffective any treatment directed to the renal infection itself. Many of these obstructions can be relieved by cystoscopic manipulations, although surgery will be required in certain cases.

Since most kidneys become infected by bacteria conveyed through the blood stream, it is essential that foci of possible infection—in the skin, respiratory tract, genitalia, and intestinal tract—be eliminated by adequate measures if the kidney infection is to be relieved and its recurrence prevented.

After underlying pathological conditions have been discovered, there still remains a relatively large group of chronic infections in which no accessory urogenital abnormality can be found. These are the cases of so-called pure focal pyelonephritis in which there is bilateral involvement, persistent or intermittent pyuria, and characteristic pyelographic findings. The treatment of these cases is chiefly medical and is frequently disappointing—sometimes requiring continuance over a period of many months or even years.

In chronic infections, nephrectomy is usually necessary when there is advanced renal suppuration. When there is still hope of saving the kidney, this is accomplished by the oral administration of urinary antiseptics, lavage of the kidney pelvis with suitable antiseptics, an abundance of fluids, attention to diet and regulation of the bowels, and the promotion of free drainage, chiefly by the use of an indwelling ureteral catheter.

The oral administration of urinary antiseptics has long been a popular method of treatment. Except in the simpler and more superficial infections, however, cures are probably rarely attained by the use of urinary antiseptics alone. Extensive parenchymal involvement, such as the multiple foci of suppuration seen in protracted diffuse pyelonephritis, is likely to prove resistant to all attempts to obtain a cure by drug therapy or by pelvic lavage through the ureteral catheter. The choice of antiseptic will depend upon the type of invading organism. The most useful antiseptics now available are the sulfonamides, mandelic acid, mandelamine, and methenamine. These are discussed in detail on pages 1162 to 1186. Penicillin, when available for general clinical use, should prove very valuable in staphylococcal infections.

The ketogenic diet (p. 1189), while efficient in a large proportion of urinary infections due to the colon bacillus group of organisms, is difficult to administer and poorly tolerated by many patients because of its high proportions of fat and carbohydrates. It therefore has a limited applicability, and has been largely replaced by sulfonamide and mandelic acid therapy.

The indwelling ureteral catheter is sometimes very useful, in cases complicated by obstruction, for the promotion of free drainage. The pyelonephritis of pregnancy, in particular, is very frequently benefited by this form of therapy. The catheters should be frequently observed to see that they are draining satisfactorily, and, if there is evidence of blockage, irrigation should immediately be instituted.

Lavage of the renal pelvis through the ureteral catheter (p. 1715) is indicated in the treatment of many subacute and chronic renal infections. The ureter is opened up by the mechanical action of the ureteral catheter, which is probably the chief virtue of lavage, although the credit is likely to be given to the antiseptic solution employed.

General measures to build up the patient's resistance, such as rest, abundance of fluids (except in certain forms of drug therapy, where fluids must be restricted to secure adequate concentration of the drug), attention to diet, and regulation of the bowels, are of great importance in the treatment of renal infections. In the simple, non-obstructed and non-complicated acute cases of pyelonephritis, Beer found castor oil to be almost a specific, and claimed very satisfactory results in innumerable cases over a period of many years. Its efficacy he believed to be due to the fact that in most of these cases there is an invasion of the blood stream from the incompletely evacuated colon.

Vaccines and bacteriophage have many supporters, but their popularity is not so great as formerly.

Surgery is indicated in certain cases for the removal of obstructions or the correction of some urogenital abnormality. In severe cases of bacillary infection, exposure of the kidney and decapsulation have been productive of rapid improvement in many instances. Perirenal drainage and drainage by nephrostomy are necessary in certain cases.

If the opposite organ is functionally efficient, a functionless pyonephrotic kidney should be removed, both to safeguard the patient's general health and to diminish the danger of involvement of the opposite kidney. When nephrectomy is decided upon, every effort should be made to put the "good" kidney in condition to assume the double burden

soon to be imposed upon it. As it has probably been doing the work of both sides for some time, this may at first seem an unnecessary precaution, but statistics show that uremia, due to failure of the function of the remaining kidney, is the most frequent cause of postoperative death in cases of pyonephrosis. Preoperative drainage of the pyonephrotic kidney, thus lessening the amount of circulating toxin carried to the healthy organ, and lavage of the other kidney, if there is reason to believe it is sharing in the infection, are advisable. When both sides are seriously affected, the only course is bilateral nephrostomy, which is rarely successful.

(3) *Pyelonephritis of Pregnancy*

Pyelonephritis of pregnancy—frequently, but improperly, termed pyelitis—is of common occurrence, and probably helps materially to account for the preponderance of renal infections in females. The condition is often bilateral. When unilateral, the right side is more likely to be affected than the left. There is always involvement of the adjacent ureter and frequently cystitis. Pus, in varying amounts, is almost always present in the urine, but unless microscopic examination of the urine is made, the milder cases are likely to go unrecognized, the rather vague symptoms being attributed to pressure of the enlarging uterus, constipation, or other factors.

Pyelonephritis occurs most often during the first pregnancy, although some women have an associated pyelonephritis with each pregnancy.

Etiology and Bacteriology. The *Bacillus coli* or allied form is the predominant organism—occurring in over 80 per cent of the cases. Other organisms occasionally identified are *B. proteus*, staphylococci, streptococci, and the gonococcus.

Hematogenous infections, from a focus in the intestinal tract, probably make up the majority of these infections; but ascending infection, by vesico-ureteral reflux, cannot be disregarded, in view of the frequency with which there is found in pregnant women a bacilluria combined with the presence of residual urine in the bladder—the latter condition favoring reflux. Colon bacilli and other infectious organisms from the female genital tract or the lower intestinal canal can ascend to the bladder up the short urethra without producing a urethritis, and, in the presence of reflux, set up renal infection.

Obstruction and stasis are the chief accessory factors in the production of any form of pyelonephritis; and in the causation of pregnancy pyelo-

nephritis stasis due to pressure of the enlarging uterus upon the ureters at the pelvic brim is undoubtedly a prominent predisposing factor.

The physiological influence of pregnancy on the urinary tract has been demonstrated not only by postmortem studies but by pyelographic and cystoscopic investigations. Such studies have definitely proved that displacement of the ureters and obstruction by pressure are regular accompaniments of pregnancy. The relation of renal infection to these changes is, however, poorly understood. Not all pregnant women suffer infection, and other preexisting or concurrent factors must operate in addition to the anatomical changes caused by the enlarging uterus.

Numerous observers (Kretschmer, Heany, and Ockuly; Luchs; Harris; Bugbee, Schumacher; Woodruff and Milbert) have demonstrated, by roentgenographic studies, that the ureters and renal pelves are regularly dilated during pregnancy, so that even under the best conditions the kidneys of the gravid woman run more chance of becoming infected than those of non-pregnant women. This characteristic dilatation of the upper urinary tract during pregnancy was noted a century ago by Pierre Rayer, who commented on the frequency with which it was associated with infection. Demonstrable dilatations may appear as early as the sixth week, but dilatation usually occurs after the third month. The ureteral dilatation is, with rare exceptions, above the brim of the pelvis. Kretschmer, Heaney, and Ockuly found dilatation of the ureters and renal pelves during pregnancy and the puerperium in 100 per cent of their cases; in 59.3 per cent there was a return to normal after 2 weeks and in 34.3 per cent after 6 weeks, while the remaining 6.2 per cent were normal after 12 weeks.

As the uterus continues to enlarge and pressure on the ureter increases, there is delay in the excretion of the kidney, associated with more or less atony of the ureter and an increasing feebleness in its response to stimuli. With more or less stasis, together with delayed emptying of the renal pelvis, ureter, and bladder, conditions favoring the production of infection are set up.

This same pathological picture of dilatation, stasis, and infection, it should be noted, is frequently seen in non-pregnant patients with uterine fibroids, ovarian cysts, and other pelvic tumors. Kretschmer and Kanter (1937), in a urographic and pyelographic study of 51 patients with fibroids, ovarian cysts, or prolapse, found unilateral or bilateral dilatation and displacement of the ureters in 33. Following appropriate surgi-

cal procedures, a restoration to normal took place in 72.5 per cent, as evidenced by postoperative pyelo-ureterograms.

Another factor that easily might influence the production of pyelonephritis during pregnancy is the congestion of the mucosa of the pelvic portion of the ureter which appears at about the third month, in association with edema of all the pelvic viscera, as well as the vagina and external genitalia. By diminishing the caliber of the lumen of the pelvic ureter and of the ureterovesical orifice, this edema increases the stasis produced by the obstructing gravid uterus.

Other etiological factors have been suggested. A pyelonephritis of infancy or childhood is believed by many to have an important bearing on pregnancy pyelonephritis (a history of such infection is fairly common in pyelonephritis of pregnancy). Renal congestion due to pressure of the gravid uterus on the venous supply of the kidneys, together with the increased work thrown upon the kidneys during pregnancy, has been suggested. Many observers feel that poor ureteral drainage, combined with intestinal stasis (due to pressure on the intestines by the uterus, sedentary habits, etc.), is a leading cause of these infections. Nephrop-tosis and its common accompaniment, enteroptosis, are very frequent in women, and it has been suggested that these, by producing stasis both in the kidneys and the intestines, may play a part in the causation of pregnancy pyelonephritis. A congenital anomaly may be the main causal factor, for an abnormal urinary tract, which functioned well in the non-pregnant state, may be easily crippled when crowded by the enlarging uterus.

Stricture of the ureter has been advanced as a frequent cause by Hunner, Corbus and Danforth, and others. Unilateral or bilateral strictures are found fairly often in pregnant women, and, when present, undoubtedly increase their susceptibility to infection. Later observers (Crabtree; Livermore) are, however, inclined to the belief that the stricture is the result rather than the cause of the infection—the pressure on the ureter at the pelvic brim so injuring the ureteral mucosa as to make it a ready lodging-place for bacteria, which set up inflammatory changes that eventually produce a stricture.

Purely focal infections, blood borne from infected cervical or perineal lacerations, or from infectious foci in the teeth, tonsils, etc., may, of course, occur in patients who have had no renal involvement during pregnancy but whose resistance has been lowered by childbirth.

Pathology. Whether the infection be hematogenous or ascending,

the ordinary pathological picture is that of an acute, diffuse, exudative inflammation involving the parenchyma, pelvis, and ureter, usually accompanied by cystitis. The ureteritis is not as a rule severe enough to injure the mucosa sufficiently to induce stricture by the formation of fibrotic tissue. Sometimes, however, the submucosa and muscularis become involved in a widespread inflammatory reaction which, if continued for any length of time, will produce a typical scar-tissue fibrosis. Like any pyelonephritis, the pathological process in the kidney may proceed to suppuration, with the production of multiple miliary abscesses in the parenchyma, or it may eventuate in an atrophic pyelonephritis. More often, however, following delivery healing ensues promptly, the inflammation being dependent largely upon obstructive changes which are transient and physiological in nature.

This point of view—that pyelonephritis of pregnancy is a transitory affection in most cases—is a prevailing one among both urologists and obstetricians. It is based on the fact that in most pregnancy infections of the urinary tract there is little evidence of renal insufficiency and hypertension, and, where such insufficiency has been demonstrated, there is prompt return of the kidneys to apparent normal function. In order to determine whether the effects of the pyelonephritis are actually as temporary as has been generally supposed, or whether there later is evidence of renal insufficiency and hypertension, Crabtree and Reid in 1940 made a clinical study of 45 cases in which the patients had had pregnancy pyelonephritis 5 to 10 years earlier, without evidence of renal pathology prior to the pregnancy. The cases were divided into 3 groups. Group I consisted of 14 cases in which there was pyuria, bacteriuria, and little or no fever. Group II consisted of 12 cases in which there was some fever and more severe symptomatology, but the patients all were tractable to treatment. Group III consisted of 19 cases in which there were severe febrile manifestations; most of these patients required cystoscopic treatment and even induced labor before there was subsidence of the acute symptoms.

Some of their more pertinent findings were as follows:

1. Through examination by intravenous pyelography, intravenous phenolsulphonphthalein excretion, concentration of the urine test, and tests for the retention of nitrogen, evidence was produced which indicated "that a high percentage of patients suffer appreciable damage to their kidneys which is demonstrable at from 5 to 10 years after the infection. For the majority, adequate renal function is present at that time."

2. The severity of the initial pyelonephritis is not, apparently, any criterion of the persistence of the infection beyond the average rate of spontaneous clearance. Of the mild cases, 5 of the 14 patients were still infected at the time of the study; while 3 of the 12 patients with moderately severe infections, and 6 of the 19 patients with severe pyelonephritis, were known to have remained infected.

3. The prognosis is grave in patients who have had both toxemic and pyelonephritic injury. Hypertension occurred in all of the 3 such cases in this series; and 2 of the 3 patients were dead 5 years after the injury.

4. Six patients with pyelonephritis showed blood-pressure readings above 150/90, associated with some evidence of renal deficiency.

5. Renal injury, in this group, consisted of injury both to the conduction channels, pelvis and ureter, and to the cortex. When there is injury to the conducting channels, the stasis of urine produced by this condition may further injure the cortex, especially when infection is still present. Stone occurred in 5 of the 45 patients studied.

It is the opinion of these experienced investigators that the pyelonephritis of pregnancy should be regarded as a progressive disease in many cases, although as yet they have no data indicating to what extent it shortens life.

Symptoms. The symptoms may be mild or they may be exceedingly severe. In general, they are similar to those in other forms of pyelonephritis (p. 1466). Many patients first notice a disturbance of urination (frequency, dysuria, urgency). Examination of the urine will usually reveal pus cells, albumin, and bacteria—generally *Bacillus coli* or, more rarely, staphylococci. Not infrequently, however, there will be no vesical symptoms other than the usual frequency of the later months of pregnancy. As a rule, there is fever (usually of low grade), with chills, sweats, nausea and vomiting, and soreness and pain in one or both loins. Marked prostration may develop. Leukocytosis of varying degree is the rule, but may be absent.

The infection may remain dormant during pregnancy, producing only mild symptoms, but may become acute following delivery; when there will be severe symptoms and large amounts of pus in the urine.

Diagnosis. Carefully compiled statistics of a number of large maternity centers indicate that a majority of the patients are between the ages of 20 and 30 years, although there is a prevailing impression—shared in by the medical profession and the laity—that very young and middle-aged primiparae are most prone to “kidney trouble.”

The diagnosis differs in no way from that in other forms of pyelonephritis, and is based on the history, physical examination, and microscopic examination of the urine. Routine urinalysis, such as is practiced by all physicians in charge of pregnant patients, is serviceable in calling attention to any kidney irregularities, but is of small aid in diagnosing the precise nature of these disturbances.

Most urologists are of the opinion that symptoms of infection and the finding of pus and organisms in the urine justify immediate urological investigation. When there is leukocytosis, fever, chills, nausea and vomiting, and right-sided abdominal pain, the infection may be difficult to differentiate from appendicitis or ovarian disease. Cystoscopy will differentiate pyelonephritis and should be done promptly.

Excretion urography is frequently helpful in diagnosing renal disturbances attending the pregnant state. Of course, if a kidney is functioning so poorly that excretory urography yields no results on the affected side, recourse to other diagnostic methods will be necessary, but even these negative results may serve a useful purpose when correlated with other findings, and excretory urography should be done when indicated.

Treatment. An increasing appreciation of the necessity of adequate prenatal care and supervision of every pregnancy, whether presenting pathological symptoms or not, will automatically reduce the incidence of evil results from the physiological alterations inevitable in the upper urinary tract even during normal pregnancy. Appropriate urinary antiseptics may assist in keeping the urine sterile when the period of obstruction and consequent urinary stasis is reached.

In general, measures advocated for the eradication of infection in the kidneys and ureters in pregnancy do not differ from those in similar renal infections in non-pregnant women. The infection can usually be controlled to full term, but cannot be cured before delivery. An uncomplicated pyelonephritis seldom necessitates the interruption of a pregnancy. Rest, suitable diet, large amounts of water (by mouth, or, if this is impossible, by hypodermoclysis, intravenously, or by rectum), alkalization of the urine, followed by oral administration of urinary antiseptics, and—above all—the establishment and maintenance of adequate drainage from both renal pelves, will, in most cases, permit the patient to be carried to full term. Drainage in these cases is best maintained by the use of indwelling ureteral catheters (Indwelling Ureteral Catheterization, p. 1716).

Failure to control the infection by the use of the above measures necessitates the termination of pregnancy, but this is uncommon. Some-

times, in unilateral conditions, such as stone, or renal or perirenal suppuration, an emergency nephrostomy or decapsulation may permit the patient to be carried to term—nephrectomy or other necessary radical surgery being postponed until after the puerperium. In grave bilateral lesions, however, interruption of pregnancy is preferable to any type of renal surgery.

Perinephritic Abscess

Definition. There has been considerable discussion regarding the proper classification of the lesion called by some a perinephritic abscess and by others a perinephric, perirenal, or a paranephritic abscess. Strictly speaking, perinephritic abscess includes only suppurations of the perinephrium—the fatty tissue between the kidney and the renal (Gerota's) fascia. If the inflammation or suppuration is outside the renal fascia, it is pararenal (paranephritis; pararenal abscess). Since, however, these lesions are indistinguishable clinically, they will be considered together under perinephritic abscess.

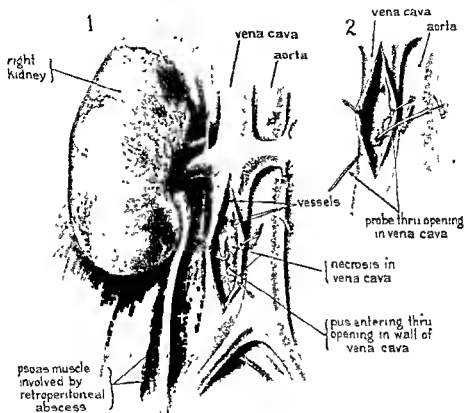
Rayer (1839) was the first to describe perinephritis. Lillenthal (1896) drew attention to the relationship between perinephritic abscess and cortical suppurations of the kidney. Israel (1905) first described renal carbuncle and pointed out its association and that of perinephritic abscess to peripheral skin suppurations.

The Perinephrium. The perinephrium is the lemon-yellow layer of fat surrounding the kidney inside the renal fascia. It was originally described by Gerota, who found no trace of it at birth, observed that it was still in a state of evolution at puberty, but found it to be fully developed in the adult. This fascia and its attachments are so located that when retroperitoneal suppuration in the pelvis travels upward it will eventually surround the kidney. It also acts to convert into a perinephric process any suppuration arising in the kidney which breaks through the latter's fibrous capsule.

Etiology and Bacteriology. Perinephritic abscesses are most commonly classified as *primary* or *secondary*. They are also grouped as *renal* or *non-renal*.

A perinephritic abscess is said to be primary (non-renal) when it originates from a focus outside the kidney. "Primary" refers, as a rule, to the metastatic perinephritic or paranephritic abscess of staphylococcic origin; but it may refer to the now rarely observed perinephritic abscess which is a direct extension from suppuration in neighboring organs, such

as the retroperitoneal appendiceal abscess or other suppuration which extends upward, or an empyema which spreads downward. The perirenal fascia extends along the ureter to the bladder, and infections may ascend along this periureteral sheath from adnexal and pelvic lesions in both sexes and be the cause of a perinephritic abscess, though this is uncommon.



Wm P Diduch 1931

FIG. 314. Case of rupture of the vena cava caused by a retroperitoneal abscess. View obtained at autopsy. (1) The vena cava has been opened, and pus is shown entering through an opening on the posterior wall (2) Shows a probe passed through the opening in the vena cava.

"Secondary" refers to those cases in which the primary lesion is in the kidney. The perinephric tissues become secondarily infected either by extension from or rupture of the renal focus. This condition is very commonly seen in cortical abscesses, carbuncle, and calculous or tuberculous pyonephrosis, but less seldom in pyelitis or pyelonephritis.

While all observers agree that there is a definite relationship between

perinephritic abscess and both the suppurative infections of the renal cortex and suppurative foci elsewhere in the body, there is considerable

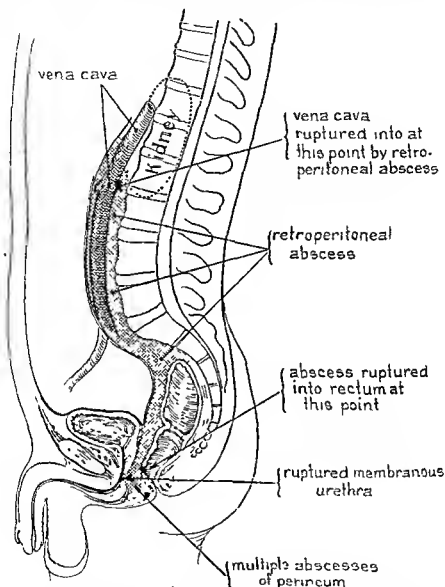


FIG. 315 Rupture of the vena cava caused by retroperitoneal abscess. Schematic drawing showing longitudinal section of the body. The membranous urethra had ruptured, followed by the formation of multiple perineal abscesses. The abscess then burrowed upward until it reached the level of the kidney. At this point it invaded the wall of the vena cava, causing rupture of the same and death.

difference of opinion as to the relative frequency of primary (metastatic) perinephritic abscess and perinephritic abscess following cortical sup

purations. There is believed to be a separate arterial supply to the perinephrium from the renal artery, and, in view of this, Vermooten, Bugbee, and other recent writers have emphasized the probability of perinephric suppuration being frequently produced by metastatic infection of the perinephrium from a superficial pyogenic focus, an acute suppurative otitis media, or a coccic suppuration in the respiratory or digestive tract. On the other hand, Israel, Beer, and many others who have made careful studies of these infections, while conceding the possibility of metastatic infection of the perinephrium, are of the opinion that operating-room and postmortem evidence points strongly to the greater frequency of perinephritic involvement from a primary focus in the renal cortex.

Trauma is probably an important predisposing factor in the development of perinephritic abscess. Even slight force, by causing rupture of the fine blood vessels in the perinephric fat, may result in the formation of minute hematomas, which provide ideal breeding-places for pus-forming organisms which may chance to be in the blood stream.

Staphylococcus aureus is the causative agent in the majority of cases. *Staphylococcus albus*, streptococci, various bacilli, and pneumococci are occasionally found. When perinephric and coccic cortical suppurations are associated, the pus from both lesions almost always contains the same organism—namely, *Staphylococcus aureus*; but when the perinephritic abscess is associated with cortical abscesses due to ascending pyelonephritis, *Staphylococcus aureus* is an infrequent finding—bacilli of the colon, proteus, pyocyaneus, Friedländer, or lactis-aerogenes groups being usually identified both in the pus and in the urine (Beer).

Incidence. Perinephritic abscess is more common in men than in women. Any age may be affected, but the age period of greatest incidence is between 20 and 40 years. A number of cases have been reported in children and a few in infants, but as a rule perinephritic and cortical renal suppurations are much more common sequelae of staphylococcic infection in adults than in children, in whom osteomyelitis is the usual sequel.

The right side appears to be affected slightly more often than the left. Bilateral involvement is rare. Hunt, searching the literature in 1924, was able to collect only 11 cases, and few have been recorded since. Twinem (1936) reported from our service a case of bilateral perinephritic abscess in a patient with polycystic kidneys. Six weeks before admission the patient (a fireman) had been struck in the left flank by a stream of

water from a fire hose. A perinephritic abscess developed on the left side first, and later another developed on the right side.

Pathology. Upon exploration, there will be found great edema of the perinephrium and a small amount of pus in early cases; but in cases of longer duration an immense abscess cavity may surround a portion or all of the kidney. Occasionally there may be detected the point in the kidney cortex whence an abscess had its beginning.

Perinephritic abscess is usually an acute condition, but may be chronic. Chronic forms of the disease follow acute attacks which may have been overlooked because of their mildness. Lowsley had a case of 9 years' duration, during which there had been three distinct exacerbations. There were three separate cavities connected by small orifices similar to those of vesical diverticula.

Symptoms. There are no pathognomonic signs or symptoms. The early manifestations are those of an acute or subacute infection in any part of the body. The onset may be sudden, with fever, chills, leukocytosis, nausea and vomiting, and prostration; or it may be gradual, and manifested mainly by general weakness and inertia and unexplained fever. Costovertebral pain and tenderness are regularly present, but do not differ from the pain and tenderness produced by stone, pyonephrosis, or advanced tuberculosis. A tender tumor develops in the loin, and palpation will reveal an indefinite mass in the flank, with rigidity and, sometimes, a "doughy" feel. There may be flexion of the thigh, making voluntary extension painful if not impossible.

Diagnosis. The diagnosis is based on the history, physical findings, and plain x-ray examination. Of particular importance are (1) a history of previous pyogenic infection (carbuncle, boil, otitis, osteomyelitis, etc.), (2) leukocytosis and unexplained fever, (3) costovertebral pain and tenderness, and (4) the palpation of a tumor in the loin. Occasionally a needle may be inserted into the suspected area and pus withdrawn.

Cystoscopy and urography are of little value. Urinalysis gives little or no help except in the relatively rare perinephritic abscess associated with pyelonephritis or pyonephrosis, when organisms (usually bacilli) may be recovered from the urine. Blood cultures are often helpful, and should always be made.

The plain x-ray is frequently a valuable aid when considered with the history and clinical course. Obscuration of the shadow of the psoas margin, effacement of the renal shadow, and curvature of the lumbar spine are all common findings—particularly the first, which is prac-

tically a constant sign. Scoliosis occurs late. Mathé has made an important contribution in his "sign," which is lack of normal mobility or descent of the kidney, as shown by a pyelogram made in the Trendelenburg and vertical postures, with displacement of the ureter due to hypertrophy of the perinephric fat or to adhesion of the cicatricial tissue of the perinephric space to the blood vessels of the renal pedicle. It is present only in perinephritic abscess, carbuncle, and cortical abscess.

Prognosis. Perinephritic abscess, particularly when associated with renal suppurations, is a grave condition. Untreated, these abscesses may rupture into the paranephric space and burrow down toward the groin or upward into the subdiaphragmatic space, or they may rupture posteriorly through the loin, or anteriorly into an adjacent loop of intestine. These extensive abscesses, once common, are now rarely seen.

If drainage is instituted early, the patient's chances of recovery without nephrectomy are good. Nephrectomy is sometimes necessary, however, if the kidney is extensively involved. Frequently, in these cases, as previously noted, the patients recover after simple incision and drainage, the cortical suppuration having already ruptured into the perinephrium. In general, the condition of a patient suffering from one of these abscesses is so grave that intervention upon the kidney, if necessary, must be deferred until the acute perinephritic condition has abated.

Treatment. The only treatment is early incision and drainage, with general supportive measures to rid the patient of his staphylococcic infection. A complicating lesion of the renal cortex may require subsequent nephrectomy or other surgery.

Replacement Lipomatosis of the Kidney

While lipid nephrosis is a relatively common finding, fibrous and fatty replacement is decidedly unusual, and was, until comparatively recently, confused with true renal lipoma. Replacement lipomatosis is seen only in a diseased kidney, and consists in an infiltration of fat which invades the renal tissues by proliferation from within. The process usually extends from the hilum and pelvis toward the periphery, until the parenchyma, which has been destroyed or atrophied by some pathological process, is completely replaced by fatty or fibrous tissue. Thus fat replacement is not a disease of itself, but merely a reparative process following renal disease.

The first mention of this condition in medical literature appears to be the account given by Baader, in 1778, of an autopsy finding of pyelo-

nephritis with stone and fat infiltration of the kidney substance. Kutzmann, in 1931, found records of but 32 cases, to which he added one of his own. Roth and Davidson found 70 cases up to 1938. This small number probably does not reflect the true incidence of the condition.

Etiology and Pathology. We do not know why fat replacement occurs in some kidney diseases and not in others, nor are we aware of the exact process by which the transformation into fat takes place. Two etiological theories have been advanced. One is that chronic inflammatory processes in the kidney stimulate hyperplasia of the perirenal and peri-

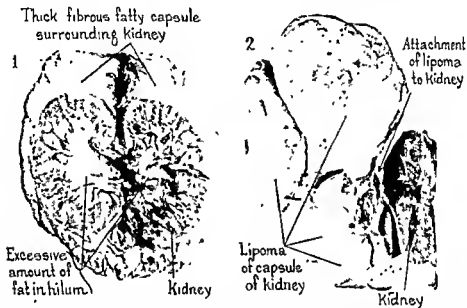


FIG. 316 (1) Section of gross specimen showing a contracted kidney with replacement lipomatosis. There is marked thinning of the cortical tissue. (2) Lipoma of the renal capsule. Gross specimen. The lipomatous mass is adherent to the lateral border of the kidney. (Christeller.)

pelvic fatty tissue, the fat cells then proliferating so as to enter the kidney through the capsule or hilum, with the result that the renal parenchyma is eventually so overwhelmed as to become atrophied. The second theory attributes the renal atrophy to the action of some unidentified destructive process, the invasion of proliferating fat being secondary to the renal injury and not its primary cause.

Inasmuch as it has long been established that the kidney is remarkably resistant to the effects of pressure, as in the case of retroperitoneal tumors, which do not seriously affect it even when they attain considerable size, it is not reasonable to suppose that renal atrophy could be brought

about by the pressure of fat alone. The postulation of some slow inflammatory process as the primary cause seems more plausible. The formation of stone, which leads to infection (or is the result of it) and injures or even destroys the renal tissue, setting up eventual pyonephrosis, would seem to be a logical etiological factor. Kutzmann found stone in 79 per cent of the cases he collected from the literature and from clinical experience. More recent writers, notably Roth and Davidson, place the incidence of renal stone in conjunction with fat replacement of the renal parenchyma at 76 per cent. Whatever its cause, fat replacement is undoubtedly a reparative process, although of such a nature that the "repaired" kidney is permanently bereft of most or all of its functional ability.

Symptoms and Diagnosis. Diagnosis has rarely been made before operation or autopsy. Apparently there are no symptoms which point definitely to this particular renal lesion. The recorded diagnoses contain many references to renal tuberculosis, and the fact that the atrophic process induced by fatty infiltration quite often performs autonephrectomy as completely as does tuberculosis would make such a diagnosis reasonable. As long-standing infection had been previously recognized in all the kidneys affected with fat replacement, pyuria was always present and excited no especial notice. There may or may not be pain over the affected kidney; but if atrophy is advanced, there will be no pain whatever, and the bladder urine will be quite normal as the unaffected kidney will be doing the work of both sides.

Pyelography is useful largely by negation. Atrophy is sometimes so complete that the contrast material cannot be injected by the retrograde method, and, of course, the functionless kidney will not excrete dyes introduced intravenously. The fact that the kidney cannot be outlined by either method indicates that it is the seat of some very grave lesion, but there will be nothing to point specifically to fatty replacement of the renal parenchyma.

Prognosis and Treatment. The prognosis for any return of renal function is hopeless, and the only effective treatment is nephrectomy.

Specific Infections of the Kidney and Renal Pelvis

(1) Renal Tuberculosis

Of all the forms of urogenital tuberculosis, renal tuberculosis is considered to be of the most importance. Its high clinical significance is due to the fact that it is of frequent occurrence, is common to both

sexes, is often bilateral, and, while occurring in all age periods, most frequently appears at the beginning of adult life, when the responsibilities of life work and parenthood are being assumed.

Though considered separately here, renal tuberculosis—like tuberculosis of the epididymis, prostate, seminal vesicle, or bladder—requires a consideration of the entire urogenital tract. Irrespective of where it starts, tuberculosis of any portion of the urogenital tract has a marked tendency to spread from one part to another and eventually to involve the entire tract unless checked by early and proper surgical treatment. In these combined lesions it is frequently impossible to tell which of the urogenital lesions is primary, though it is generally believed that the infection most often starts in the kidney. It must also be remembered that tuberculosis is a constitutional disease, urogenital infection being only a local manifestation.

Incidence. Statistics are difficult to obtain in regard to the incidence of renal tuberculosis. Kapsammer, in a careful study of 20,777 routine autopsies, found 191 cases of renal tuberculosis, or a little over 1 per cent; 67 of these were unilateral and 124 bilateral. Kuester found 158 cases, or about 3 per cent, among 5,338 routine autopsies. Hobbs, in 1,000 autopsies on patients dying from pulmonary tuberculosis, found clinical evidence of renal tuberculosis in 16.2 per cent; microscopic tuberculosis was found in 32 per cent of a small series of kidneys from these cases. Caulk reported that 30 per cent of all surgical lesions of the kidney studied in his series were tuberculous. Approximately 30 per cent of all nephrectomies performed at the Brady Foundation, of the New York Hospital, have been for tuberculosis.

Etiology and Pathogenesis. Renal tuberculosis is practically always hematogenous in origin. The consensus of opinion today is that ascending tuberculous infection by way of the ureter or lymphatics does not occur, and that tubercle bacilli reach the kidney through the blood stream. The primary focus is believed to be in the lungs, tonsils, or intestinal tract. The patient may be fortunate enough to develop satisfactory resistance, so that the primary lesions are completely cured or become quiescent; or the infection may progress in the primary area and its lymphatics until finally the tubercle bacilli invade the blood stream. If the invasion of the blood stream is massive, a generalized miliary tuberculosis results, in which the kidneys may participate. If the organisms enter the blood stream in showers, the phagocytic cells of the body may overcome them. Frequently, however, the tubercle

bacilli lodge in the bones, joints, or soft tissues of the body, setting up the secondary lesions of tuberculosis. In the meanwhile, the primary lesion in the lungs, tonsils, or intestines may have healed or become quiescent. If the patient's general and local resistance is sufficient, the secondary lesion in the kidney (or elsewhere) may heal; otherwise, it progresses, with the eventual production of destructive tuberculous lesions.

It is also possible for renal tuberculosis to be blood borne from a secondary lesion elsewhere (in a bone, joint, the liver, a urogenital organ etc.); or both the renal lesion and other secondary lesions may originate from the same primary focus in the lungs, tonsils, or intestinal tract.

The pathogenesis of renal tuberculosis has been studied by Medlar and Sasano (1924), Eberbach (1927), Harris (1930), Band (1935), and others. It is now generally assumed that a bacilli-laden embolus is carried into the kidney in the blood stream and accidentally lodges in a glomerular capillary tuft. The bacilli are of low virulence and grow slowly, without completely obstructing the blood channel. The glomerular focus may be walled off; or a few bacilli may reach the capsular space and multiply while being washed slowly along the proximal convoluted tubule until they reach a favorable soil for growth in the thin arm of the medullary loop (Eberbach); or the bacilli may reach the medulla by way of the fine efferent glomerular capillaries (arteriolae rectae) which radiate into the medulla. It has also been suggested (Nitch, 1925) that the primary cortical lesion spreads to the medulla by the lymph stream.

The initial glomerular lesion may heal, continue to grow slowly, or, if the bacilli are unusually virulent, may develop into the main lesion (rare). It has been suggested (Lieberthal) that the abundant vascular supply of the kidney, and the large caliber of its capillaries, give a peculiar immunity to the tubercle bacilli which may aid in the healing of these microscopic lesions.

The medullary lesion usually grows relatively fast. Medlar believes that even these medullary lesions may heal; but frequently such a tubercle will spread and finally open into a renal tubule or papilla, discharging its contents into the renal pelvis. If the medullary lesion is near a calyx, clinical symptoms and secondary kidney infections are likely to appear early; if near the base of a pyramid, it may involve a substantial portion of the parenchyma before giving rise to pelvic infection. When the medullary lesion communicates with the kidney pelvis, the patient has

a clinical, destructive tuberculosis; and pathological evidence of the healing of such a lesion has not been reported (Chronic Renal Tuberculosis, p. 1494).

Opinions differ as to whether the initial lesions in the kidney are predominately cortical or medullary. Ekehorn states that lodgment of the tubercle bacilli usually occurs primarily in one of the pyramids. Eberbach, who carefully studied the entire question of the pathogenesis of renal tuberculosis, contends that clinical and pathological observations indicate that highly virulent organisms attack the kidney cortex primarily and later may extend to the medulla, while the less pathogenic group meet with cortical resistance and only gain a foothold when they reach the medulla or pelvis, and that this is true of tubercle bacilli: highly virulent tubercle bacilli give rise to a miliary tuberculosis characterized by multiple cortical lesions, while markedly attenuated bacilli produce chronic medullary lesions. Medlar examined autopsy specimens of kidneys from 30 patients who had died of pulmonary tuberculosis without manifesting clinically any renal involvement. Forty-four separate kidneys were examined, and 367 definite tuberculous lesions found in them were studied by means of approximately 100,000 sections. Of these, 277 (about 75 per cent) were in the cortex, 40 (11 per cent) were in the medulla, while 50 (13 per cent) were cortico-medullary. Only in the case of the smaller lesions was it possible to determine the precise point of origin.

The smaller lesions were of two main types. The most common of these types was of vascular origin within the capillary tuft of a glomerulus, within a capillary between the convoluted tubules, or within a capillary between the collecting tubules in the pyramids. Of these points of origin the most common was within a glomerulus and the least common in a pyramid. In the earlier glomerular lesion several instances were found in which one half of the glomerulus was involved while the remainder was normal. The second type of small lesion had its origin within the lumen of a tubule. These lesions were found with about equal frequency in the lower point of the loop of Henle and in the collecting tubules in the pyramid. They always subtended an ulcerating tuberculous lesion of some portion of the kidney substance. It appears that this type of lesion is always secondary to a vascular lesion which has developed to a point where destruction of tissue has supervened and tubercle bacilli have been discharged into the lumen of a tubule.

The Question of Initial Bilateral Involvement. The chief stumbling-block to all who hold to the theory of blood-borne infection has always been the apparent predominance of unilateral renal tuberculosis. Many investigators, however, take the position that the infection in the begin-

ning is a bilateral implantation, but that the disease develops in only one kidney. Small cortical tuberculous infections are set up in both kidneys; these, however, do not always develop into destructive lesions, but are frequently overcome in the incipient stage, due to the abundant blood supply of the kidneys. One or both sides may heal spontaneously, or one or both may progress and produce the clinical forms of unilateral or bilateral renal tuberculosis respectively.

Of the many disputed points concerning renal tuberculosis, none has been more discussed, *pro* and *con*, than this question as to whether, at the outset, one or both kidneys become infected. Van der Vuurst de Vries, in Belgium, contends that at the outset all renal tuberculosis is bilateral, adding, "In the greater number of cases one side is spontaneously cured." Band, in Scotland, found that in many cases where no symptoms had appeared during life to indicate that one kidney had shared in the tuberculous infection of its fellow, at autopsy small areas of tuberculous invasion could always be found in the kidney thought to be sound. Medlar states positively that bilateral infection is the rule.

On the other hand, a number of equally competent observers hold that renal tuberculosis is unilateral from the onset. Hinman states:

The assumption of initial bilaterality in all cases is unwarranted. There is no more reason to assume the infection of both kidneys, because the infection is blood-borne, than to assume that both knees must be infected, because one is, or both femurs or any other two similar parts of the body. Furthermore, staphylococcal renal infections, which are always hematogenous, are usually unilateral, even when acute and fulminating.

Although the evidence thus far adduced seems to us to favor initial bilateral involvement, definite proof of such initial bilaterality in all cases is still wanting.

Spontaneous Healing of Initial Lesion. Until fairly recently it was generally believed that every case of renal tuberculosis progressed to complete destruction, and that healing never took place except by auto-nephrectomy.

Most observers are agreed that a chronic, destructive renal tuberculosis probably never heals without complete renal destruction.

As to the question of spontaneous healing of the early, symptomless lesions, opinions differ. Some investigators believe that all renal tuberculosis is steadily progressive from the outset, and that healing never occurs. In common with many observers, however, we feel that the preclinical lesions may undergo spontaneous and complete cure under

certain circumstances—an idea advocated almost two decades ago by Chute. R. S. Harris contends that minute foci of tuberculosis may develop in the kidney but later undergo healing just as do tubercles in other tissues. "It would be extraordinary," he argues, "were the kidney, of all the tissues in the body, the only one incapable of ever overcoming a tuberculous infection. . . . There is evidence that early, small lesions at least have a strong tendency to heal." Braasch, of the Mayo Clinic, has put himself on record, as follows: "We formerly believed that renal tuberculosis never healed spontaneously. However, experimental and clinical evidence in recent years would lead us to believe that very early renal infection with tuberculosis, without necrosis or destruction of the kidney substance, might permit of spontaneous healing, providing the patient's resistance is great enough." Thomas and Kinsella (1927), after a clinical and pathological study of sanatorium patients, came to the same conclusion.

Medlar is of the opinion that, when tubercle bacilli reach the kidney of a highly resistant patient, instead of caseation taking place the bacilli will be destroyed by a hyperplastic process. His previously mentioned postmortem examination of 30 patients, who died of advanced pulmonary tuberculosis without ever having had urinary symptoms, revealed renal tuberculosis in 22, with scars indicative of healing in 17. After caseation, a reparative process generally sets in, during which giant cells appear in large numbers; therefore, if such cells are detected, it is definite evidence that healing is taking place. Many types of lesions have been found in a single kidney. Mononuclear tubercles, tuberculous abscesses, areas of caseation, scarred areas infiltrated with lymphocytes and with one to many giant cells present, and scars devoid of lymphocytic or mononuclear leukocytic infiltration, have all been observed in one organ. The pathological processes found in such kidneys represent lesions of different age and severity, and the scars represent the healed stage in an area where the tubercle bacilli have been successfully overcome. In 5 of the 30 cases studied, nothing but scars was found, which this author considered proof that under favorable conditions complete healing of renal tuberculosis does take place.

Pathology. Two main groups of tuberculous renal lesions are to be distinguished: (1) medical lesions, which occur in connection with generalized miliary tuberculosis; (2) surgical lesions, which may be subdivided into (a) preclinical lesions, and (b) clinical lesions.

Acute Miliary Tuberculosis (Medical Lesions). Miliary tubercu-

losis of the kidney occurs in connection with generalized miliary tuberculosis, is almost always bilateral, is unbenefited by any type of surgical or medical treatment, and is usually fatal. Tubercles, 1 to 2 mm. in diameter, are generally scattered throughout the renal substance. Caseation and cavity-formation do not occur. There is a coexistent parenchymatous nephritis. The urine contains tubercle bacilli, but very little pus. The patient usually dies from generalized dissemination of the disease, or he may eventually die from uremia. In infants and children under 5 years of age, renal tuberculosis is more likely to be of this bilateral, medical, miliary type, and the younger the child, the more rapid is the dissemination of the disease and the poorer the prognosis.

Preclinical Lesions. The preclinical stage of renal tuberculosis is the initial, silent period from the time the first tubercle bacillus is implanted in the kidney until the involvement of the bladder gives rise to urinary symptoms. Tubercles are found in the cortex and medulla and do not communicate with the renal pelvis. It is now believed by many investigators that these initial, bilateral lesions often heal spontaneously without being discovered. Commonly, however, they progress (in one or both kidneys) into well-advanced destructive lesions before producing symptoms.

Little that is definite is known regarding the pathological picture at this stage of the disease. The active stage may be brief, and the lesions so minute that they cannot be detected clinically. They produce no urinary symptoms, and neither the renal function tests nor the pyelograms show evidence of abnormality. Tubercle bacilli may be recovered from the urine at this silent stage, but the diagnosis is probably seldom made outside of sanatoria for tuberculosis, where urine examinations are made routinely on patients with no urinary symptoms.

It has been indisputably shown that a tubercle bacilluria without pus frequently occurs in all forms of extrarenal tuberculosis. Since it has been established that a normal kidney never filters tubercle bacilli (or other organisms) out of the blood into the urine, it is now generally believed that the existence of a tubercle bacilluria, with or without pus and blood, always indicates tuberculous changes in the renal parenchyma (Bumpus, Medlar, Harris, Hinman, Greenberger, Thomas, etc.). Such experienced observers as Thomas and Kinsella assert positively that they have never failed to find tuberculous lesions in one or both kidneys when tubercle bacilli had appeared in the bladder previous to nephrectomy or autopsy. Medlar demonstrated by experimentation that pa-

tients suffering from tubercle bacilluria invariably presented tuberculous lesions—microscopic or otherwise—in the kidney. Others, notably Wildbolz, maintain that a tubercle bacilluria may be excretory without there being any tuberculous changes in the kidney.

Clinical Lesions (Chronic Renal Tuberculosis). Chronic renal tuberculosis may take various forms, which tend to merge one into another, so that there is seldom a clean-cut picture of pathological change. Active lesions of different age and severity, as well as healed lesions, may be observed in a single kidney.

Clinical renal tuberculosis is much more often unilateral; but bilateral involvement is relatively common, the infection usually being more extensive in one kidney than in the other. Much loss of function, due to destruction of renal tissue, is usually followed by compensatory enlargement of the other kidney.

The great majority of cases of renal tuberculosis are some form of *caseocavernous* tuberculosis. The focal lesions in the kidney tend to undergo caseation, forming a tuberculous abscess, which is *closed* or *open*—in the latter case communicating with the renal pelvis or a perinephritic abscess. These lesions may be multiple, and tissue destruction may rapidly progress to pyonephrosis. On the other hand, if the patient's local and general resistance is good, a moderate-sized parenchymal abscess or tuberculous area may be held in check for years. Such an area may be surrounded by sufficient connective tissue to prevent it, temporarily, from connecting with the calyces or pelvis, so that tubercle bacilli and pus cells cannot reach the urine. The lesion may be chiefly parenchymal, or it may involve mainly the renal pelvis and ureter. In the later stages there is marked lobulation and destruction of renal substance.

There is a less common *sclerotic* form of renal tuberculosis, in which the organ does not show gross lesions when exposed, only its size being markedly reduced. Microscopic examination will show tubercle bacilli in the tissues, and the urinary tract lower down will give a typical picture of tuberculosis.

Lieberthal postulates three definite stages in the spread of renal tuberculosis, as follows: (1) in the first stage, metastatic tubercles appear in the renal substance. (2) In the second stage, a caseous ulcer appears on a renal papilla and a descending infection of the urinary mucous membrane follows. (3) In the third stage, an ascending reinfection of the previously uninvolved portions of the renal tissue ensues; in this

ascending reinfection the arterial system of the kidney plays a leading role.

The original medullary lesion is most often located close to the tip of a papilla, so that it early infiltrates the neighboring calyx. If the lesion originates deep in the renal parenchyma, at the base of a pyramid, it may attain a considerable size before reaching the pelvis by extension. The



FIG. 317. Section of kidney showing long-standing tuberculosis. The multiple abscesses are well walled off in nature's attempt to heal the lesion.

chronic medullary lesion is secondary to an initial focus in the cortex, which itself may have healed.

The caseous papillary ulcer is the first lesion in the course of a tuberculous infection of the kidney which can be clinically diagnosed. A lesion embedded in the renal substance cannot discharge organisms into the urinary stream, so usually gives no evidence of its presence; but the papillary ulcer constitutes an open focus which soon discharges tubercle bacilli into the renal pelvis and down the ureter into the bladder. The caseous crater of such an ulcer provides an ideal nursery for more tubercle

bacilli. "The constant crumbling of the necrotic center," says Lieberthal, "leads to a prolonged dissemination of tubercle bacilli into the renal pelvis, as a result of which a descending infection of the urinary mucous membranes, as well as an ascending reinfection of the previously uninvolved areas of renal tissue, takes place."

A typical lesion in the epithelial layer of the mucous membrane appears first as an isolated, minute, yellowish tubercle, surrounded by a zone of deep, angry red. This lesion spreads by granulation, the granulations being typical of tuberculous processes everywhere: red-brown plaques the size of a pea or larger, over which yellow tubercles are scattered, the whole area appearing rough and loosened from the underlying tissue. The surrounding mucosa is normal in appearance. The ulcers are formed by the breaking down of these plaques by caseation of the tubercles within the granulations. The ragged sharp edges of the base are undermined, and the entire ulcer is covered with a grayish deposit. These ulcerations may be found anywhere in the kidney pelvis or its calyces. At first confined to the epithelial layer, the pathological process soon descends beneath the epithelium to the muscular layer. Edema, round-cell infiltration, and, eventually, induration of all the affected tissues occur. The tubercles break down and merge, and caseation becoming more sidespread, the entire affected area soon presents the appearance immediately recognizable as advanced renal tuberculosis—that is, dirty-gray in color and moth-eaten and ragged in outline.

The deeper tuberculous cavities develop through the pressure of retained urine and the erosive process, which is continually augmented by tubercle bacilli that are carried from the centers of caseating ulcers already formed to lodge behind strictures due to contraction and induration of scar tissue. When such stricture-formation has partially or entirely occluded the ureteral outlet, stagnation of infected urine will rapidly carry the invading organisms to any unaffected parts of the kidney, and previously immune renal papillae will soon be involved in the general destruction. Stagnant urine, confined by strictured lumina, induces further caseation and consolidation, until the entire interior becomes filled with a putty-like substance, or hardens down into a concrete-like mass. The kidney is reduced to a mere shell, showing scarcely any of its normal characteristics. The interior of the shell is subdivided into cavities for which greatly stretched columns of Bertin furnish thin-walled partitions. Such an organ falls an easy prey to secondary infection, and infected hydronephrosis or pyonephrosis completes the pathological picture.

Side by side with the advance of the tuberculous process one may see healing lesions and mark nature's attempts to repair the ravages of the invading organisms. The destructive elements slowly gain the upper hand, however, and though healing takes place at some points, new foci are constantly being set up, and the formation of scar tissue steadily lessens the functional ability of the kidney as a whole and thus accelerates its degeneration and final atrophy.

Calcification is common in association with caseation. The entire kidney may be calcified, or there may be a single, dense area of calcifica-

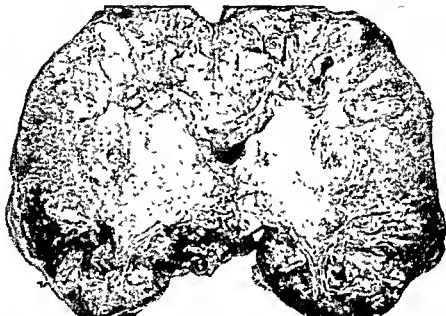


FIG. 318. Advanced tuberculosis of the kidney. Note large abscess cavity in the upper pole. The remainder of the kidney shows considerable granulation tissue, several walled-off areas, and other evidence of nature's attempts to repair the ravages of the invading organisms.

tion; but more commonly there will be single or multiple groups of scattered, small calcareous deposits.

Other renal abnormalities, such as calculus, hydronephrosis, tumor, or polycystic disease, frequently coexist with tuberculosis.

Perinephritis is a not uncommon complication of renal tuberculosis, and occurs when the tuberculous process involves the surface of the cortex and the fibrous capsule. The resulting adhesions, as many a surgeon has learned, add a decided element of difficulty to operative intervention on the tuberculous kidney. Perinephritic abscess also occurs with relative frequency.

Ureteral and Vesical Involvement. Tuberculous involvement of the

corresponding ureter and the bladder is the rule once the medullary tubercle has ruptured into the renal pelvis. The ureter becomes dilated, and its walls thickened and hardened. Ordinarily, it is when infection has descended to the bladder, setting up a cystitis, that the patient comes to the urologist and the renal tuberculosis is discovered. Sometimes the disease halts at the calyces, without invading the pelvis; under these circumstances the kidney may be completely destroyed without producing infection of the lower urinary tract. Again, the ureter may be strictured early in the invasion, in which event the renal lesion may remain undetected because no urine, tuberculous or otherwise, can escape on that side and the opposite kidney will secrete normal urine into the bladder. The unaffected kidney will increase in size and output as it is compelled to assume the function of its diseased fellow. The ureter may also be occluded by caseous material. Occlusion of the ureter, by calcification or caseation, results in so-called *autonephrectomy*—complete destruction of the kidney by the disease. The final result will be either a pyonephrosis, or a “putty” kidney (in which the caseating process entirely replaces the renal parenchyma), or a completely calcified or atrophied kidney. Approximately 0.5 per cent of tuberculous kidneys undergo complete calcification (Gibson, 1935).

The pathological changes in the bladder, in tuberculosis of the kidney, have been described under Diseases of the Bladder (p. 1026). Briefly: The bladder becomes infected and ulcerated, and a resulting interstitial cystitis develops, which causes contracture of the bladder and diminution of its capacity. As a result of this marked bladder involvement, the integrity of the opposite ureterovesical sphincter is partially lost, permitting urinary reflux up the healthy ureter and the implantation of tubercle bacilli in the wall of the ureter or renal pelvis. Quite often a stricture is found to involve the lower portion of the opposite ureter, and a hydro-nephrosis develops in the previously healthy kidney.

Symptoms. Although renal tuberculosis is occasionally fulminating, with severe initial symptoms, in the majority of cases the disease develops slowly. The early lesions produce no symptoms, and the disease is discovered accidentally in routine examinations by the finding of tubercle bacilli in the urine or suggestive changes in a pyelogram.

Because of the insidiousness of the onset and the fact that the primary symptoms are not alarming, patients usually seek medical aid at a comparatively late stage of the disease. Symptoms have generally been

present for 6 months or more—frequently for many years. Many patients seen by the urologist have been treated for varying periods for cystitis. One of ours had had mild urinary symptoms and tubercle bacilli in his urine for 35 years before he came under our observation.

The chief symptoms of renal tuberculosis are: (1) frequency and urgency of urination, (2) pain when the bladder is emptied, and frequently (but not always) a constant, dull ache in the lumbar region, (3) pyuria, and (4) hematuria.

Frequency of urination is the most common complaint, occurring in over 80 per cent of cases. There is often an associated urgency and pain in the bladder. These symptoms tend to increase in severity, and fail to respond to medical treatment. At first the frequency may occur only during the day, or solely at night, but eventually is present both day and night. It is usually due to tuberculous ulceration of the bladder, and indicates that the renal tuberculosis has been present for a long time. In some cases frequency may be due to a contracted bladder, or, in early cases without vesical involvement, to a tuberculous pyelitis. Again, it may be due to polyuria, it being well known that the tuberculous kidney often secretes large amounts of pale urine.

Although bladder symptoms predominate as a rule, many patients describe their first symptom as a constant dull, aching pain, or feeling of heaviness, in the lumbar region of the affected side. In a few this is the only symptom. When renal tuberculosis is well advanced, there may be renal colic due to stricture or blockage of the ureter by caseous material or blood clots.

Hematuria is important, and is sometimes the first symptom. It may be either renal or vesical. A few drops of blood may be noted at the end of each urination, or the blood may be microscopic in amount, or it may be sufficient to give the urine a smoky appearance or even a mahogany color. Smoky urine is due to a combination of blood and pus cells emanating from an ulcerated area, and would thus appear only when the disease is well advanced. Periodic hemorrhages sometimes occur, the urine being clear in the intervals between attacks; this is probably more characteristic of relatively mild tuberculous processes than of severe and rapidly spreading infections. As a rule, copious bleeding does not occur until ulceration is well advanced.

The urine is usually acid and clear except when clouded by pus or blood cells. Albumin of pyogenic origin is regularly present.

Constitutional symptoms are frequently entirely lacking. Usually the more widespread the lesion and the longer the duration, the greater the likelihood of general symptoms. One of the first noticeable signs may be a diminution of strength and a tendency to tire easily, or a feeling of lassitude and a lack of initiative, or a gradual loss of weight. Other general symptoms occasionally complained of are chills and sweats, a slight daily fever, gastrointestinal disturbances, nervous irritability, and insomnia.

Diagnosis. *Preclinical Lesions.* The ideal objective is, of course, the diagnosis of renal tuberculosis in the early stage, before there is extensive destruction of renal tissue, or ureteral and vesical involvement. The diagnosis of the early, non-destructive lesion in renal tuberculosis is, however, always difficult and often impossible, and is probably seldom made outside of sanatoria for tuberculosis. Because they produce no symptoms, these preclinical lesions are rarely seen by the urologist. Such a lesion may heal, or may progress to a well-advanced destructive lesion before giving symptoms. During this silent stage, which may last for years, tubercle bacilli are frequently present in the urine.

Gilbert J. Thomas believes that if all tubercular patients are subjected to a routine urinalysis every 3 months, with complete urological study if cellular elements are found in the urine, all lesions of renal tuberculosis may be discovered early and many arrested by conservative methods, or, if this is not possible, appropriate treatment may be instituted before there is involvement of the lower urinary tract. Such an examination should also be made if a patient between 16 and 40 years of age, without apparent tuberculosis, shows pus or unexplained albumin in the urine on routine examination.

Neither renal function tests nor pyelograms are likely to be of value in the diagnosis of these early lesions.

Clinical Renal Tuberculosis. When the advice of the urologist is sought, urinary symptoms are almost always present, indicating that the renal lesions are usually well advanced.

Urologists differ considerably as to how much data is necessary to make a diagnosis and outline the treatment in a given case of renal tuberculosis. Since the diagnosis is often exceedingly difficult, and since it is essential to determine not only that renal tuberculosis exists, but whether it is unilateral or bilateral, and the extent to which destruction has occurred, we subject patients to a thorough routine examination and complete cystoscopy. Although the routine examination often indicates

the nature of the illness, a comprehensive idea of the lesion and how it should be treated cannot be gained until cystoscopic examination, pyelograms, and renal function tests of each kidney have been made. Pyelograms show the characteristic changes, indicate the extent of infection, and frequently suggest, in a general manner, the function. The phenolsulphonphthalein tests and urea excretion from each kidney are valuable in appraising the renal function. Blood chemistry, especially urea nitrogen estimations, are helpful. The diagnosis is established primarily by the pyelographic findings, with evidence of decreased renal function in advanced cases.

(1) *History and Physical Examination.* A carefully elicited history is of the greatest importance. It may be suggestive or entirely negative. The clinical renal tuberculosis seen by the urologist differs somewhat from that observed in a sanatorium for tuberculosis. Only a certain percentage of patients (from 20 to 40 per cent in various reported series) give a history or show evidence of any preexisting tuberculosis. Although renal infection is secondary to a focus elsewhere in the body, by the time the urologist is consulted the primary focus has often healed so completely that it cannot be detected by the customary physical and x-ray examinations. A history of antecedent or concurrent tuberculous disease elsewhere will, of course, be of great aid in leading to the correct diagnosis.

The family history may also be helpful.

The age of the patient has an important bearing. Well over half of the patients suffering from chronic renal tuberculosis, in any series of cases, are between the ages of 20 and 40 years. In our own series, approximately 70 per cent of these surgical tuberculous kidneys have occurred in patients of this age group, and this percentage coincides with the findings of most observers. It is now recognized that renal tuberculosis occurs in infants, children, and adolescents more frequently than has generally been believed. Of 4,698 cases of unilateral surgical renal tuberculosis reviewed by Mathé, 565 (12 per cent) occurred in patients aged 1 to 20 years; 20 cases (0.42 per cent) were in infants aged 1 to 5 years, 51 cases (1.08 per cent) were in children 5 to 10 years, and 494 cases (10.5 per cent) occurred in adolescents aged 10 to 20 years. The more widespread interest in urology in children, and the possibility of making routine urological studies of suspected cases due to the perfecting of small-caliber child cystoscopes, is responsible for the increasing number of diagnoses of juvenile renal tuberculosis.

Although renal tuberculosis shows no marked affinity for either sex, in most of the reported series there has been a slight predominance of male patients. In a series of 97 patients treated by nephrectomy in our clinic, 50 were males and 47 females (Henline, 1933).

In a young patient of either sex, a history of frequency, nocturia, urgency, and polyuria, in the absence of other demonstrable causes, should make one suspect and search for tuberculosis, particularly if the voided specimen contains microscopic blood. Infants and children, as well as adults, suffering with chronic cystitis and persistent or relapsing pyuria, should be carefully examined for tuberculosis.

Many of the patients seen by the urologist are healthy-looking individuals, with no evidence of a generalized infection, either active or latent. In a series of 40 patients with bilateral renal tuberculosis, treated at the Brady Foundation, only 15, when first seen, had demonstrable tuberculous lesions elsewhere or gave a history of any previous signs of tuberculosis. Epididymitis had developed in 6 patients when first observed, and was found to be present eventually in 14 of the 21 male patients. A careful physical examination may reveal evidence of a healed tuberculous lesion or the presence of an active one, either of which should arouse suspicion, in a patient with urinary symptoms, that the patient may be suffering from renal tuberculosis. In males, a most careful examination of the genital tract should be made. Palpation of the epididymes, and rectal palpation of the prostate and seminal vesicles, may reveal nodulation of one or all of these organs. This physical examination must be supplemented with x-raying of the chest.

(2) *Urine Examination.* Examination of the bladder urine should, and in practice regularly does, precede cystoscopic procedures, as in most cases it is the findings of such examination that lead one to suspect renal tuberculosis. The urine of a patient with renal tuberculosis practically always deviates from the normal. Usually it is highly acid. The pathological elements most frequently found are: pus, albumin, blood (gross or microscopic), and casts. A sterile pyuria in an acid urine is presumptive evidence of tuberculosis. The demonstration of tubercle bacilli in urine is a relatively simple matter, and the finding of organisms constitutes a positive diagnosis. Repeated examination of the bladder urine is, therefore, the most important preliminary step of examination. Repeated interval examinations must be made in suspected cases because infected kidneys will transmit tubercle bacilli, pus cells, and blood cells into the urine intermittently, so that the urine may be negative one day and positive the next.

There are three chief methods of examining the urine for tubercle bacilli:

(1) Acid-fast staining of the sediment of a 24-hour specimen, collected by a method which excludes the smegma bacillus, which also is acid-fast. Acid-fast organisms will then denote tuberculosis. (This is the most common and valuable method.)

(2) Guinea-pig test. If no tubercle bacilli are found in the stained sediment, specimens are centrifuged and the sediment injected into a guinea-pig. If the guinea-pig test is positive, an attempt should again be made to isolate the organism from the urine. A single positive guinea-pig test, alone, is not sufficient for a diagnosis.

(3) Cultural identification of the tubercle bacillus in the urine. Cultural methods and guinea-pig inoculations are of about equal value in the identification of tubercle bacilli in specimens of urine. Cultures are less expensive and are done in less time, but require more technical skill. Cultures may be used to supplement guinea-pig inoculations when the stained sediment is negative.

(3) *Cystoscopic Examination.* A complete cystoscopy is, we feel, necessary for the accurate diagnosis of renal tuberculosis and the outlining of treatment. This includes a thorough examination of the bladder; catheterization of both ureters (when possible), with the collection of urine specimens from the bladder and from each kidney for culture, urea estimation, microscopic examination, and guinea-pig inoculation; estimation of the function of each kidney by the phenolsulphonphthalein test; and the making of plain roentgenograms of the bladder, ureters, and kidneys with the x-ray ureteral catheters in position, followed by the making of bilateral pyelo-ureterograms.

Inspection of the bladder frequently reveals findings which are so characteristic that the diagnosis of tuberculosis is self-evident (Tuberculosis of the Bladder, p. 1028). The vesical changes secondary to renal tuberculosis vary from slight inflammatory changes around a ureteral orifice to extensive ulcerations, with or without contraction of the bladder. As a rule, extensive bladder tuberculosis means far-advanced renal disease. The lesions are most often seen around either or both ureteral orifices or on the trigone. In the earlier cases, there is merely a reddened, thickened area, with or without rigidity of the lips of the ureteral orifice. As the disease progresses, the redness deepens in hue and the normal glossy appearance changes to dullness. The lesions may extend about the bladder in the form of a diffuse inflammation, or as scattered, irregular areas of granulations. Ulceration subsequently en-

sues, with the development of typical shallow, irregular tuberculous ulcers. Tubercles may develop in the mucosa as minute yellowish spots surrounded by a hyperemic base. Widespread ulceration with infiltration of the bladder wall results in a contracted bladder, with diminished vesical capacity. As a rule, the lesions are most marked about the ureteral orifice on the side of the renal tuberculosis. Many of these ureters become patulous ("golf-bole ureter") owing to the extensive scar-tissue formation in the wall of the ureter.

Badly inflamed or contracted bladders make cystoscopy difficult and painful. In such cases, thorough anesthetization is necessary, and it is sometimes advisable to employ spinal anesthesia.

(4) *Ureteral Catheterization.* Ureteral catheterization should be done whenever possible, extra precautions being taken to avoid carrying infection into a previously sterile kidney. The bladder should be distended as little as possible, so as to avoid vesico-ureteral reflux.

Catheterization of one or both ureters may be impossible, due to stricture of the ureter. Of 40 cases diagnosed as bilateral renal tuberculosis in the Brady Foundation, it was impossible to catheterize either ureter in 14, and one ureter in 7 others (Henline, 1939). In such cases, reliance must be placed primarily on evidence from the intravenous urogram. (The 29 kidneys removed in this series were all proved to be tuberculous.)

The proper collection and examination of separate specimens of urine (by microscopic study, guinea-pig test, and culture) are of particular importance in the diagnosis of renal tuberculosis. Pus in a ureteral, catheterized specimen of urine, with a positive report of tubercle bacilli, either by stain, guinea-pig test, or culture, constitutes a positive diagnosis of tuberculosis in the kidney from which the specimen came. Failure to demonstrate tubercle bacilli in the catheterized specimen is not, however, conclusive proof of the absence of tuberculous infection, as tubercle bacilli appear in the urine intermittently. As a rule, pyuria is present on one side only, and the finding of organisms on both sides does not always indicate bilateral involvement. Only one kidney may be diseased, but a reflux up the normal ureter may contaminate the urinary specimen from the healthy kidney, and may mislead one into assuming that a bilateral renal tuberculosis exists.

Finding tubercle bacilli in the catheterized specimen is of the greatest help in making a diagnosis, and we search diligently for them by stained smears and guinea-pig inoculations. However, we do not hesitate to

diagnose renal tuberculosis even though the organism has not been isolated from the urine.

Renal function tests are valueless in the diagnosis of early renal tuberculosis, with very slight destruction of tissue, but in the more advanced cases usually seen by the urologist they are helpful in deciding when surgery is indicated. Diminished renal function, as determined by the phenolsulphonphthalein test, the indigo-carmin test, urea estimation, or excretory urography, gives one an idea of the approximate destruction in the kidney. Tests of relative renal function are sometimes of great value in helping to decide whether a lesion is unilateral or bilateral when organisms are found in the urinary specimens from both sides.

(5) *Roentgenography.* The plain roentgenogram is of little value except in the demonstration of old calcified lesions. Tuberculous shadows usually occur in multiple small, scattered clusters of varying density; but there may be a single small area, or several small, localized areas, or a large, irregular area involving most of the kidney. The ureter also may be calcified.

Bilateral urograms are necessary before a complete diagnosis of the presence and extent of destructive lesions of tuberculosis can be made. Both excretory and retrograde pyelograms are often necessary.

Excretory urography is a distinct aid in some cases, but cannot replace retrograde pyelography. It gives considerable information regarding the function of each kidney, and is helpful in outlining the renal pelvis, but the pelvic outline obtained by this method is not so distinct as that obtained by retrograde pyelography. The early or small destructive lesions of renal tuberculosis, which are outlined in the retrograde pyelogram, are not visualized in the excretory urogram. Excretory urography is most useful when it is impossible to cystoscope a patient or to catheterize either ureter. In these cases urography would otherwise be impossible.

Bilateral retrograde pyelo-ureterograms should be obtained routinely if the ureters can be catheterized. The practice of making bilateral pyelo-ureterograms in renal tuberculosis has been criticized on the ground that backflow readily occurs and organisms might be disseminated by the blood stream and produce a generalized tuberculosis. In common with many other urologists, we have made innumerable bilateral pyelograms in renal tuberculosis without evidence of miliary infection, meningitis, or other ill effects.

Gilbert J. Thomas and his co-workers, who have more opportunity

of observing the earlier lesions of renal tuberculosis than the average urologist, state:

We know of no method of examination that will reveal the tiny macroscopic ulcerative or destructive lesions of tuberculosis in the kidney parenchyma as constantly as the pyelogram. By this method we have been able to demonstrate small ulcerative lesions and parenchymal abscesses when a specimen of urine from the same kidney did not reveal bacilli of tuberculosis. . . . The lesions of renal tuberculosis that may be demonstrated in a well-filled retrograde pyelogram are the ulcerative lesions, parenchymal abscess, and tuberculous pyonephrosis. These can be differentiated only by well-filled retrograde pyelograms, which will visualize any deformity of the kidney pelvis or parenchyma.

In our own practice, we have come to rely for diagnosis primarily upon the pyelographic findings, with evidence of marked diminution in function in advanced cases (Roentgenography of the Genito-Urinary Tract, Renal Tuberculosis, p. 154). The early calyceal or papillary ulcer appears in the pyelogram as a small moth-eaten area in the border of a minor calyx. Two common types of advanced renal tuberculosis may be diagnosed by the pyelogram. The first appears as a large, dilated, irregular renal pelvis and ureter. This type of tuberculous kidney usually has very poor function and is the end-result of a long-standing, continuously destructive process in a patient with little or no resistance against the disease. The second type is characterized by shagginess and irregularity of the major and minor calyces, without much increase in the size of the renal pelvis, often with calcifications in the kidney substance, and a small, irregular, beaded ureter. This latter group includes those cases which show a tendency toward healing, and usually has a better resistance to the tuberculous infection. When there is closed ulceration or caseation in the parenchyma, tuberculosis may be advanced yet manifest no pelvic deformity.

Prognosis. It is generally felt that the prognosis in cases of unilateral tuberculosis that have been subjected to nephrectomy is good; while in cases of bilateral disease, and of unilateral lesions treated medically, the outlook is uniformly poor, although the expectation of life may be for many years. In recent years, however, there have been reported many cases that have been diagnosed as bilateral renal tuberculosis in which the patients have been either much improved or clinically "cured" by the use of surgery. In our own practice, many patients with bilateral lesions, who formerly would have been considered hopeless, have been definitely benefited and their lives prolonged by combined surgical and medical treatment. Tuberculosis is among the most unpredictable of

diseases, and apparently "hopeless" cases with bilateral lesions often live a surprisingly long time even under medical treatment alone. However, from the standpoint of mortality and longevity the nephrectomized patient has, we feel, a decided advantage in both unilateral tuberculosis and those cases of bilateral involvement where one kidney is destroyed and the other one slightly infected.

Much depends upon the individual patient's powers of resistance. In general, the patient with unilateral renal tuberculosis, who has the diseased kidney removed before there is serious involvement of the bladder, has a much better end-result than the patient in whom the diagnosis is made late and the bladder tuberculosis is extensive. However, even advanced lesions in the bladder frequently heal under medical treatment, once the infectious focus in the kidney has been removed. If active pulmonary tuberculosis also is present, the outlook will naturally be less favorable than when there is hope that removal of the diseased kidney will eliminate the chief source of infection.

Treatment. *Preclinical Tuberculosis.* Unilateral or bilateral non-destructive renal tuberculosis—the so-called preclinical lesions—should be treated medically. When tubercle bacilli are found in the urine from one or both kidneys, but there is no urographic evidence of renal destruction and no demonstrable change in the comparative function of each kidney, the patient should have the benefit of careful medical care in the hope that the kidney will heal. If, during medical treatment, a destructive lesion supervenes—as manifested by pyuria, marked diminution of function, or urographic evidence of renal destruction—surgical measures become necessary. These early, symptomless lesions, as already noted, are likely to go unrecognized except in sanatoria for the treatment of tuberculosis, where patients undergo periodic urinalysis along with other tests. They are seldom encountered in private practice, as patients seek medical aid only when definite symptoms have appeared.

Clinical Tuberculosis. In the selection of treatment, the first consideration is whether the tuberculous process is limited to the urinary tract, or whether active tuberculosis is also present in other organs of the body, usually the lungs. If the kidney lesions are a late complication of an active pulmonary tuberculosis which is progressing through the body, the prognosis is grave and the debility is such that surgery is contraindicated. These patients are best treated in sanatoria for tuberculosis.

When the active tuberculosis is limited to the genito-urinary tract, the paramount considerations are (1) whether the renal lesions are unilateral or bilateral, and (2) the extent of the disease in the kidney or kidneys.

(1) *Unilateral Lesions.* The treatment of choice in unilateral chronic tuberculosis, with clearly evident destruction of the kidney or pyonephrosis, is nephrectomy followed by proper medical treatment. As much of the ureter as possible should be removed through the nephrectomy wound. If, however, the ureter is grossly infected throughout its length, a complete nephro-ureterectomy should be done, if the patient's general condition warrants it; or a secondary ureterectomy should be performed later. The prognosis in cases thus treated is good, unless there is very extensive involvement of the bladder.

Formerly it was rather generally believed that even slight unilateral lesions were best treated by nephrectomy, but the present tendency is to treat by medical measures patients with early unilateral lesions and little evidence of kidney destruction.

Although nephrectomy for tuberculosis is rarely an emergency operation, it is our practice to remove the offending organ as soon as possible, unless the patient's general condition contraindicates surgery. Even in the presence of an active pulmonary tuberculosis, or activity of tuberculosis elsewhere, it may be advisable to remove the kidney. A destructive, infected, caseous lesion serves as a focus of infection. Prompt removal of this focus may enable the patient better to control his other lesions, if any are present, and may prevent the dissemination of the toxins or tubercle bacilli from this area. Failure to remove, or delayed removal of, a unilateral destructive lesion may result in the hematogenous conveyance of tubercle bacilli to the opposite kidney, or the development of toxic nephritis and nephrosis. Marked bladder involvement may permit a reflux up the healthy ureter, which, in turn, becomes infected. In order that these sequelae may be prevented, if possible, we remove the partially or completely destroyed organ as soon as possible after the diagnosis has been made.

Occlusion of the ureter by caseation or calcification is of fairly common occurrence in renal tuberculosis. It has been our personal observation that in practically every instance of so-called autonephrectomy, where the kidney was subsequently removed, examination showed the tuberculous process to be still active, even though the ureter was completely occluded. Although the renal lesion may be closed off from the bladder, it usually remains pathologically active, and, being a focus of infection and a hazard to the patient's future health, should be removed.

(2) *Bilateral Lesions.* In recent years a much larger percentage of bi-

lateral infections has been discovered. In the majority of cases there is one badly destroyed kidney, while the other is only slightly infected.

Competent urological opinion is divided concerning the treatment of these cases. One group believes that the patient with bilateral chronic renal tuberculosis is best treated by medical means, and that surgical treatment is contraindicated except under special circumstances, such as uncontrollable hemorrhage from one kidney, severe pain, or obstruction of one ureter, resulting in the production of a closed tuberculous abscess.

Others advocate the removal of a completely or partly destroyed kidney, when the other is only slightly infected, in the belief that the patient should be given every chance by removing an infectious focus which can only be a liability in his efforts to build up his bodily defences. With this latter group we are in accord. The finding of a definitely destroyed tuberculous kidney on one side and a functionally efficient mate is evidence enough, we believe, for removal of the destroyed kidney. The mortality in bilateral lesions that do not have the benefit of surgery is very high. Removal of the badly infected kidney has frequently provided a starting-point for postoperative treatment that has arrested the disease in the remaining kidney.

In general, when the pyelogram shows a destructive tuberculous lesion in one kidney (particularly if the function be markedly diminished), and the opposite kidney shows satisfactory function and slight or no urographic evidence of disease, we remove the badly infected kidney at once, even though some tubercle bacilli may be found in the urine from the opposite organ. To delay the removal of such a lesion, while repeated search for tubercle bacilli from a functionally and pyelographically normal contralateral kidney is being made, seems to us unjustified. In these bilateral cases, where surgery is considered advisable, supplementary medical treatment is more efficacious *after* the infectious focus has been removed.

Not all patients with bilateral renal tuberculosis should be subjected to operation. In the presence of bilateral non-destructive lesions, surgery is not indicated (Preclinical Lesions, p. 1493). Medical treatment is also indicated when the bilateral lesions are of equal severity, as proved by urograms and functional tests, or when the function of the less diseased kidney is markedly decreased or insufficient to carry on life.

Occasionally a patient is seen with bilateral areas of calcification and

a fibrotic form of tuberculosis. These calcifications and the lack of evidence of destructive caseation and infection indicate that nature has already attempted to heal the infection and that the patient's resistance is good. These patients may go for years under medical care, with little progression of the disease. Surgery is not indicated.

Nephrostomy is sometimes done when there is bilateral infection, but we advise against this procedure under ordinary circumstances.

Drainage of a tuberculous hydronephrosis is rarely indicated. The resulting fistula never heals, and the operation—except as a life-saving measure—should be discarded. If the other kidney will sustain life, a hydronephrotic tuberculous kidney should be removed.

Treatment of Associated Perinephritic Abscess. The treatment of a perinephritic abscess occurring in association with unilateral or bilateral renal tuberculosis is immediate surgical drainage. If the patient's general condition is poor, only incision and drainage of the abscess should be done. The performance of nephrectomy under such circumstances is attended by considerable risk.

Postoperative Care. We have no justification for ever calling renal tuberculosis "cured." Although many patients, following nephrectomy, are able to return to their regular occupations and modes of life, all writers are emphatic regarding the need of continued observation of these supposedly "cured" cases.

Medical care, sometimes over a period of many years, is indispensable in the postoperative care of renal tuberculosis, as well as in the treatment of patients suffering from bilateral inoperable tuberculosis, and should be carried out by one thoroughly familiar with this work. This phase of treatment has been considered at length under Treatment of Inoperable and Postoperative Urogenital Tuberculosis (p. 1196).

Postoperative Complications. *Pain in the Remaining Kidney.* Pain in the remaining kidney, following nephrectomy, is a distressing symptom in many patients. This probably is due to the compensatory hypertrophy and increased blood supply to this kidney, with resultant tension of the renal capsule. Pain may also be related to obstruction due to a ureteral stricture. Dilatations of the ureter of the remaining kidney may relieve renal pain, or decrease the signs of infection by affording better drainage.

Delayed Wound Healing. A lumbar sinus is present on leaving the hospital in a majority of the cases. These usually heal fairly promptly

with medical care. Some of these wounds, however, remain open and discharge for years, more or less incapacitating the patient.

The exact cause or causes of these persistent sinuses and disturbances in wound healing has not as yet been determined. They are usually attributed to (1) gross contamination of the wound by spilling of pus containing tubercle bacilli at the time of nephrectomy, (2) residual tuberculosis in the remaining capsule or ureter, or (3) actual tuberculous nodules in the region of the pedicle. Beer believes that the essential underlying causation is a traumatic bacteremia induced by the operator, which leads to a deposition of tubercle bacilli in the vascular muscle wound and in the traumatized deeper tissues.

Diffuse Miliary Tuberculosis; Tuberculous Meningitis. Diffuse miliary tuberculosis, pulmonary tuberculosis, and tuberculous meningitis not infrequently develop as terminal stages in patients with renal tuberculosis. These lesions occur with about equal frequency in all tuberculous patients. Death from these causes may occur soon after surgical or diagnostic procedures on the urogenital tract, or months or even years later. When these manifestations occur immediately after such procedures, death is often attributed to trauma incidental to urogenital manipulations. It is our belief that urological surgical and diagnostic procedures seldom cause dissemination of tuberculosis, or hasten the fatal outcome, when reasonable care is taken and inhalation anesthesia avoided.

Henline and Bray (1938) carefully reviewed the literature regarding the cause of death (immediate and remote) in patients who have had renal surgery for tuberculosis, and also studied 25 cases from the Brady Foundation, in which the patients had had nephrectomy and had subsequently died, after periods varying from several weeks to many years. They concluded that, while patients who have had nephrectomy for renal tuberculosis quite frequently develop miliary, pulmonary, or generalized tuberculosis, and occasionally tuberculous meningitis, it is probable that death in these cases results from the gradual progression of the tuberculous infection, and that the surgical and diagnostic procedures have little or no influence in the development or acceleration of these terminal stages of the disease. Patients seek medical advice because their urinary symptoms are becoming more exaggerated, and it is probable that the increasing severity of the symptoms is a manifestation of a progressive tuberculous infection in the presence of a lowered general resistance.

(2) *Gonorrhea*

Incidence. Gonococcal pyelonephritis is very uncommon. Simmons, in a careful review of the literature in 1922, found only 24 cases of proved gonococcal infection of the kidney on record. Birkhaug and Parlow, in 1928, collected 33 cases, all but 5 of which they regarded as doubtful because of the absence of fermentation and serological tests.

Inasmuch as gonococcal infection is exceedingly common, and renal and ureteral gonorrhea very rare, it is reasonable to assume that the type of epithelium lining the ureter and kidney pelvis is unfavorable to the growth of the gonococcus, which shows marked preference for columnar epithelium.

Etiology. As with other forms of renal infection, gonococcal pyelonephritis is probably blood-borne in most cases. However, the possibility of carrying infection from below upward at the time of ureteral catheterization cannot be disregarded, and such transmittance must always be rigidly guarded against.

Diagnosis. The clinical picture is similar to that of pyelonephritis due to other organisms. A history of gonorrhea previous to the appearance of symptoms pointing to renal infection is suggestive.

The diagnosis rests upon the demonstration of a Gram-negative intracellular diplococcus in the catheterized specimen of urine from the affected kidney, plus positive identification by serological or fermentation reactions. Mixed infections are common.

Treatment. The treatment is ureteral catheterization and renal pelvic lavage, with eradication of the infection from the rest of the urinary tract. The oral administration of the sulfonamides and other measures advocated for the cure of gonorrhea and its complications are described under Gonorrhea, Treatment (p. 717).

Extensive pyonephrosis may make nephrectomy necessary.

(3) *Syphilis of the Kidney*

There is a general impression that syphilis of the kidney is of decidedly infrequent occurrence. Reports of cases are seldom encountered in present-day medical literature, and text-books barely mention the subject. There is more than a probability, however, that syphilitic nephritis is not so much rare as unrecognized.

Pathology. Involvement of the kidney in the early stage of the general infection—that is, during the first year—takes the form of an acute nephritis, the clinical picture of which is usually sufficiently char-

acteristic to lead an experienced observer to apply the regular biochemical tests which will demonstrate the luetic nature of the nephritis even if there have been no other indications of a syphilitic infection. Most of these patients, however, are first seen by general practitioners, who ordinarily are not trained in the fine points of syphilitic diagnosis and are, therefore, unlikely to have these tests applied to a patient who apparently is suffering from some non-specific form of renal inflammation.

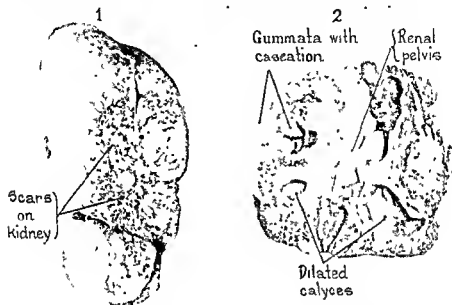


FIG. 110. Syphilis of the kidney. (1) Photograph of specimen of a kidney showing scars. (2) Section of a kidney showing scarred tissue. Male, 50.

The syphilitic nature of the subacute or chronic nephritis occurring during the later stages of the disease may easily escape detection even by an expert, unless other evidences of tertiary syphilis also are present.

Dowling (1927) has said that when one considers the march of events in syphilis, it is not surprising that the response to the infection of a particular organ or tissue is generally more or less explosive in character in the early period, with a tendency to spontaneous resolution, and, on the contrary, more sluggish in the later stages, with little or no tendency to recovery without treatment. One would expect, therefore, an acute nephritis of comparatively short duration in the early stage, and in the

later stages a subacute or chronic type which, untreated, would run a chronic course—and this, as a rule, has been the actual sequence of events in most of the reported cases.

In the initial stage of the systemic infection, for a few weeks subsequent to the appearance of the primary lesion the invaded tissues develop a high degree of sensitivity, and set up the best resistance possible to this unaccustomed irritation. The secondary manifestations represent a "culminating explosive reaction" of the extra-sensitive tissues, the result of which is the destruction of large numbers of spirochetes, which soon gives a false semblance of having overcome the spirochetal invasion entirely. Syphilologists maintain that once the secondary stage is passed, no further invasion of spirochetes takes place. Tertiary manifestations are caused by a renewal of spirochetal activity—the organisms, which have lain quiescent after their escape from the wide mortality of their fellows, now emerging to renew the attack upon the tissues, but this time producing a reaction of a different quality. Any tertiary syphilitic lesion is much more difficult to cure than one properly treated in the initial or secondary stage. The skin lesions of the early stages, for example, though violent, are easily controlled; while the gummas which appear in the tertiary stage are often highly resistant and of a much graver import. In the kidney, the lighting up of a dormant infection in the later stage of the disease evokes a less explosive response than is seen in nephritic involvement occurring earlier in the disease. The renal infection becomes a chronic process, running a protracted course.

Symptoms and Diagnosis. Two characteristics distinguish syphilitic nephritis occurring in the secondary stage of the disease from the more common forms of nephritis: (1) the immense amount of albumin present in the urine, and (2) the rapid onset and early tendency to uremia. Backache and the edema of the extremities follow the usual rule, being prominent in some cases and mild or absent in others. The diagnosis would be suggested by a definite history of a primary luetic infection, the appearance of nephritis at, or just before, the setting in of other secondary manifestations of the infection, and the elimination of other causal factors. Besides the albumin, the urine will contain an abundance of casts—epithelial, granular, and waxy—together with a sprinkling of fat droplets. A feature that distinguishes syphilitic nephritis from other forms is that, notwithstanding the marked albuminuria, renal permeability shows little, if any, impairment. The phenolsulphonphthalein

test usually gives practically normal returns, even when clinical signs point to extensive renal impairment.

The symptoms of syphilitic nephritis occurring in the tertiary stage of the disease are much less positive. Many cases of chronic syphilitic nephritis are probably never diagnosed because other tertiary lesions are concurrently present with symptoms so much more striking that when the nephritis yields to treatment its true nature is never suspected. The majority of chronic syphilitic kidney infections are discovered by chance. The urologist, or possibly the family doctor, treating the patient for a renal complaint, either observes clinical evidences of syphilis or has a Wassermann test done as a routine procedure, and, after eliminating other possible causes, is led to the conclusion that the nephritis he is dealing with has a luetic origin. A patient seen by Dowling had suffered from "chronic Bright's disease" for 5 years before a tertiary syphilitic ulceration of the soft palate appeared, and the possibly luetic nature of the nephritis was for the first time suspected. Sometimes the patient presents himself with a moderate albuminuria and an occasional shower of casts—discovered, as a rule, when he applied for life insurance. When no other cause for the albuminuria can be found, a carefully elicited history may reveal facts suggestive of a syphilitic infection in the past for which no adequate treatment was ever received, and a Wassermann test upon the blood or spinal fluid may confirm the suspicion.

Chronic syphilitic nephritis runs a protracted course, with no tendency to spontaneous resolution and with little or no tendency to improve when the patient is placed under the ordinary treatment for nephritis. The albuminuria is less marked than in the acute nephritis of the earlier stages of syphilis. The course of the disease is relatively benign, in that vascular changes either do not occur at all or make their appearance very late, for in spite of the urinary symptoms, the blood pressure remains normal or but a trifle elevated—an important differential point. The condition is almost always bilateral.

The diagnosis, therefore, is based upon the history, thorough physical examination, the Wassermann test, cystoscopy, and, in certain cases, the therapeutic test. If physical examination reveals no foci of infection or other probable cause of the renal disease, and if the blood pressure is within normal limits, and blood chemistry tests show no marked pathological changes, and the blood Wassermann is consistently negative, recourse should be had to a Wassermann test upon the spinal fluid. It

should be emphasized, however, that a strongly positive reaction may take place in an individual suffering from nephritis which is definitely known to be due to factors other than syphilis.

The most striking feature of syphilitic nephritis is the almost magical response to anti-luetic treatment. Very cautious application of the therapeutic test is, therefore, probably the surest means of diagnosis in suspicious cases.

Prognosis. The outlook for the patient suffering from syphilitic nephritis is, on the whole, better than that of one whose nephritis is due to other etiological factors. Under appropriate treatment, even cases of fairly long standing clear up rapidly. An extensively destroyed kidney can not, of course, regain its original anatomical integrity.

Treatment. If the luetic nature of the kidney infection is promptly recognized, vigorous anti-syphilitic treatment can be applied without delay. However, the well-known evil effects of heavy metals upon renal tissue make most therapists hesitant about prescribing standard measures for the control of syphilis. The only possible means of finding out whether anti-luetic treatment will be beneficial or injurious is to try it. Therefore, in suspected but not positively diagnosed cases, the anti-luetic treatment should be very cautiously applied, and if good results accrue—confirming the therapeutic test—the treatment can be pushed to the limits of tolerance. Careful observation is perhaps more essential in renal syphilis than in any other form. The treatment should preferably be in the hands of both urologist and syphilologist.

(4) *Bacillus Typhosus Infection of the Kidney*

The typhoid bacillus, though normally propagating in the intestinal tract, may be carried by the blood stream to almost any part of the body, including the kidneys. Pyuria in typhoid fever was reported upon from Johns Hopkins University as far back as 1895, but it was not until 1925 that Patch directed the attention of urologists to the relative frequency of typhoid pyelonephritis and the serious menace to the health of the community presented by the "carriers" of typhoid-infected urine.

About this same time Kirwin, working in a Southern clinic, frequently isolated the typhoid bacillus in making routine urinalyses. The close resemblance of this infective agent to the colon bacillus makes differential diagnosis especially difficult, because the colon bacillus is the most frequent cause of pyelonephritis and, unless special attention is paid to staining and other means of bacteriological test, the presence of typhoid in the kidney will not be discovered.

With steady progress in the control and elimination of enteric typhoid, the incidence of renal typhoid is bound also to decline. However, it is still seen often enough to make its recognition of importance in the differential diagnosis of kidney infections.

Pathology. Typhoid infection of the kidney may be primary, or it may be secondary to the enteric form of the disease. Only a few cases of infection limited solely to the kidney are on record—the latest being that reported by Reimann in 1938.

The lesions most often found in typhoid kidney are acute bilateral cortical and interlobular areas of suppuration, with pyelitis, ureteritis, cystitis, and, sometimes, perinephritic abscess. The condition may progress to a chronic pyonephrosis of one or both kidneys. It may well be that some of the supposed bladder infections with *Bacillus typhosus* are actually secondary to a focus in the kidney.

Symptoms and Diagnosis. The diagnosis is established by the finding of typhoid bacilli in the urine.

When the infection is limited to the kidneys, the symptoms may be entirely misleading, since they do not differ from those of other types of pyelonephritis. If the urine is examined promptly, the presence of the bacilli will be detected, if the examination is properly carried out, and the true nature of the infection thus determined. All the earlier recorded cases were autopsy findings, and it is only in comparatively recent years that efforts have been made to demonstrate renal infection apart from systemic invasion. Sometimes when a diagnosis of pyonephrosis has been made, operation will show that the organism responsible for the collection of pus in the kidney is the *Bacillus typhosus*.

Treatment. In general, the same therapy is employed as for other types of bacillary invasion of the kidney, although the profound prostration of the typhoid-fever patient adds a hazard to the use of some drugs which would be useful in other types of pyelonephritis. Suppuration and abscess-formation call for drainage or, if extensive, for nephrectomy.

(5) *Gas Bacillus Infection of the Kidney*

Gas bacillus infection of the kidney is rare, if the paucity of case reports is an adequate criterion; but its serious import, when it does occur, warrants calling special attention to the importance of early recognition and treatment.

Historical. The first case to be reported appears to be that of Goebel (1895), in connection with a pyelonephritis. Subsequently, cases were reported by Williams (1896), in connection with a suppurative pyelitis;

Kelly and McCallum (1898) and Doering (1907), in connection with pyonephrosis, and Weintrob and Messeloff (1927), in renal sarcoma. In 1928, Ferrier and Bliss published a most interesting account of the finding of *B. aerogenes capsulatus* in the center of a renal calculus in a patient who developed gas gangrene of the operative wound. Three cases were reported from abroad by Knapper (1929), Howald (1930), and Meyer (1932).

Rathbun (1931), in his report of heminephrectomy of the left half of a horseshoe kidney, provided an instructive account of the complications of renal surgery which this organism is capable of setting up. In 1934, B. W. Turner reported 2 cases, one following nephrotomy for stone and the other following nephrectomy for renal stone with cortical abscesses. In the same year a case of gas bacillus infection following induced abortion, eventuating in uremic nephritis, was presented in Paris by Harvier, *et al.* Mencher and Leiter (1938) reported 7 cases from Mount Sinai Hospital (New York); these followed operations upon the kidney or ureter for tuberculosis (3 cases), renal or ureteral calculus (4 cases), renal neoplasm (1 case), and renal cyst (1 case).

To these 20 cases collected from the literature we would add a recent personal case, which shows the rapidity with which the infection spreads and the necessity of prompt recognition and treatment.

W J S., male, aged 46 years, had a nephrotomy for the removal of a large stag-horn calculus. The operation was done in the usual manner, without any complications, bleeding being controlled by ribbon gut. The peritoneum was not opened.

On the day of operation he had a chill and his temperature rose to 104 degrees by rectum. The following day his rectal temperature was 106.2. Blood culture was negative. On the second postoperative day he was given a blood transfusion.

When examined at about 4 p.m. on the second postoperative day, there was edema of the scrotum with a normal appearing wound and slight drainage around the nephrotomy tube. Examination at 7 p.m. showed a large, gangrenous area of the scrotum, with swelling at the site of the wound, extending below the iliac crest and down toward the pubis. Smears and cultures were positive for gas bacillus. He was taken immediately to the operating-room. Reopening of the operative incision freed considerable gas from the tissues, which were necrotic. Multiple incisions were made through all the areas of crepitus down to the scrotum, releasing large amounts of gas. Drains were placed and the entire area irrigated with peroxide. Four vials of therapeutic dose of antitoxin were given and supportive treatment administered in the form of infusion, caffeine, and neo-prontosil. In 2 hours the gangrene had spread down to the ankle and further incision was made and drains placed. In 30 minutes it had spread down the entire foot and toes. The patient expired at 2.00 a.m., which was approximately 10 hours after the first area of swelling and crepitus was noted. No autopsy was permitted.

Etiology and Bacteriology. Gas bacillus infection is usually due to the activities of the *Bacillus aerogenes capsulatus* (*B. welchii*, *B. perfringens*, *B. phlegmonis capsulatus emphysematosae*). The *Vibrio septique*, discovered by Pasteur, and the *B. hystolyticus* are also capable of gas production. Other forms of bacteria found in conjunction with those known to be gas-producing are thought to be secondary factors in the production of the condition in that they consume the oxygen in the wound area which otherwise would act to prohibit growth of the anaerobic organisms.

Different observers have shown that the source of contamination, in the cases complicating renal and ureteral surgery, may be in (1) the skin, (2) operative materials, such as contaminated catgut, (3) the lower intestinal tract, (4) urine, pus, or urinary calculi. It is well known that the *B. aerogenes capsulatus* is frequently harbored normally in the rectum, and it has been suggested by Menchen and Leiter that during mobilization of the kidney and ureter, lymphatics from the bowel may be opened in the stripping away of the peritoneum, thus allowing organisms to enter the traumatized retroperitoneal area. Gas-producing organisms have been recovered from the pus and urine of numerous patients with renal or perirenal infection, and have also been isolated from urinary calculi by Ferrier and Bliss and by Mencher and Leiter. The crushing, during delivery, of a stone containing the infectious organisms might readily act to set up a postoperative gas-bacillus infection.

In 1935, Mario Fortunato, of the University of Naples, carried out certain animal experiments which tended to show that the kidney is usually highly resistant to invasion by *B. aerogenes capsulatus*, and it is only when the organ has been traumatized, or its integrity destroyed by disease, that the infection can gain a foothold.

Pathology. Two factors are necessary for propagation of the organisms: (1) injury, which devitalizes the tissues, and (2) the cutting off of the oxygen supply. So long as the circulation about the wound remains unimpaired, the development of gas bacilli will be kept in check. When the tissue is necrotic, the bacteria multiply and spread with great rapidity, infiltrating the invaded tissues and producing multitudinous air spaces from which an inflammable gas, of a sweetish, "decaying" odor, escapes. Eventually the entire affected area breaks down into an indistinguishable mass of eosinophiles and bacteria of different orders, but still studded thickly with the characteristic air-spaces.

Symptoms. The earliest symptom is an inordinate rise in temperature.

More characteristic but somewhat later signs are discoloration of the skin, a thin, purulent or mucosanguineous exudate from the wound, edema of the tissues, crepitation, and, finally, profound toxemia. Pain is not a conspicuous symptom. The presence of gas in the tissues about the wound is a practically constant feature.

The incubation period for gas-bacillus infection is from 1 to 5 days (averaging 3 days), and crepitation is a fairly late sign. If the patient is to be given a fair chance of recovery, therefore, the diagnosis should be made before crepitation is felt.

Diagnosis. Any patient who has a sharp rise in temperature shortly after operation should receive a careful inspection of the wound, as well as a general physical examination. Discoloration, edema, or crepitation in the region of the wound calls for immediate reopening and exploration of the wound, and the making of smears and cultures. The escape of gas can easily be detected on section, or when pressure is made with the flat of the hand in the direction of the wound. The organisms are usually readily demonstrated. Blood cultures are taken.

Prognosis. The prognosis is always grave. In a few of the reported cases the infection was relatively mild, but as a rule such infections are very severe and prostrating. The chances of a favorable outcome are directly dependent upon early recognition and institution of proper treatment, although even this may fail to save the patient (as in our own case). It is encouraging to note, however, that the exceedingly high mortality of the earlier cases (practically 100 per cent) is being steadily lowered.

Treatment. Treatment consists in immediate wide opening of the wound and free incision of all affected areas. Multiple drainage tubes are placed for continuous irrigation with peroxide and oxygen. Large doses of polyvalent serum are administered, and adequate supportive treatment—in the form of blood transfusions, infusions, caffeine, sulfatherapy, etc.—is given, as required. Experimental study indicates that the new drug, penicillin, may prove of great value in these infections.

(6) *Echinococcus Disease of the Kidney*

Echinococcus disease (cysticercus; hydatid cyst) is usually considered under the head of renal cysts, but inasmuch as the causal agent is an animal parasite, its proper inclusion would seem to be with infections and infestations of the kidney.

Etiology. Echinococcus disease is caused by a small tapeworm,

Taenia echinococcus, a member of the class Cestoidea of the phylum Platyhelminthes. It is an intestinal parasite of the dog, and infects human beings only when they are in very close contact with dogs and sheep, cattle, or swine—the usual intermediate hosts. It enters the various organs of man in the larval stage, forming the so-called hydatid cysts. Kidney involvement is relatively rare, the liver being the site of predilection.

Echinococcus disease occurs most frequently in the cattle and sheep-raising districts of Australia, Iceland, New Zealand, Argentina, Uruguay, the northern part of Africa, and Southern Europe. It is much less common in the United States and Canada. Magath (1937) found records of 482 cases of hydatid disease in the United States and Canada, the great majority of which occurred in immigrants who probably acquired the disease in foreign countries.

The *Taenia echinococcus* in the adult stage is from 5 to 8 mm. long. It consists of a rounded head with a double row of hooklets, and a ribbon-like body composed of three segments each of which, when mature, is bisexual. The second and third segments are the propagating portion of the worm.

The eggs, containing hooked embryos of the tapeworm, are taken into the digestive system of sheep or cattle on ingested foliage upon which the dog's excreta have been deposited, or in contaminated water, and are conveyed to man through water or raw vegetables contaminated by cattle or dogs. They enter the dog again in the ingested entrails and other offal of slaughtered cattle. The interruption of this vicious circle is comparatively easy in sections where the water supply is protected and cattle are slaughtered under regulations which prevent dogs getting access to the refuse, which explains the infrequency of the disease in modernly equipped wool and cattle-growing communities.

When the ova are taken into the alimentary tract of the human or animal host, the capsule containing the hooked embryos is dissolved by the action of the digestive juices. The freed embryos burrow their way through the intestinal wall, eventually reaching the portal circulation, whence they are carried to various tissues. Wherever the embryo lodges it develops into a hydatid cyst, which may become of enormous size. As the portal circulation always conveys it to the liver, the preponderance of hepatic cysts is readily understandable. Renal cysts are uncommon, as the embryos seldom progress as far as the kidney without being obstructed.

Inside the primary or mother cyst are developed daughter cysts from

the walls of which are formed numerous scolices with characteristic booklets. When the dog, the host, eats these scolices, which develop into adult tapeworms, the life cycle of the parasite is completed.

Incidence of Renal Hydatid Cyst. The incidence of renal location is given by Craig and Faust (1937) as from 2.01 to 4.74 per cent. Fewer than 35 cases of renal echinococcus disease have been reported as occurring in the United States and Canada (23 up to 1929, Livermore). Two cases (not reported) have been seen by us at the New York Hospital. Craig and Lee-Brown, of Sydney, Australia, reported 16 personal cases in 1928, 11 of which were in males and 5 in females.

The left kidney is involved more frequently than the right. Men are affected about twice as often as women.

Pathology. Completely developed renal hydatids vary considerably in size, and in man may attain the size of a child's head. They are usually spherical in shape, unless influenced by pressure. The lower pole is more often the site of hydatids than the upper pole.

The cyst wall consists of an external cuticular membrane and a very delicate internal germinative layer, and may attain a thickness of 1 mm. It is from the inner surface of this germinative membrane that the brood capsules are formed. The cyst is filled with a colorless or yellowish fluid, having a specific gravity of 1.006 to 1.015, and containing sodium chloride, sodium phosphate and sulphate, sugar, inosite, and albumin. Scolices are often found free in the hydatid fluid. In man, daughter cysts are frequently formed within the mother cyst, either from the germinative layer or from the brood capsules or scolices; these have the same histological structure as the primary or mother cyst.

The cyst may be closed or open—that is, communicating with a calyx or the renal pelvis.

The growth of the cyst is eccentric, extending from the point in the cortex where the embryo originally lodged and gradually pressing upon the neighboring glomeruli and tubules, causing atrophy and eventual destruction of these structures. When the cyst has become so large that it can no longer be contained within the cortical substance (an insidious process which may take as long as 15 to 20 years), it will rupture into a calyx or the renal pelvis, or it may burst and expel its contents into some neighboring organ or tissue (rare).

Multiple hydatid cysts of the kidney are rare—a single cyst, located in the cortex, being the usual finding. Exceptionally, they may occur in the medullary tissue or in the fatty capsule. Herrera-Vegas reported a

case of a 12-year-old girl who had 14 cysts of various sizes in the left kidney, an extraordinary finding inasmuch as children seldom have renal hydatids and multiple cysts are rare.

The kidney may be primarily infected, or it may be infected in conjunction with other organs, such as the liver and spleen.

Symptoms. The growth of a hydatid cyst is exceedingly slow, and symptoms usually are not present until the cyst has attained considerable size. The most common complaints are of pain in the kidney area, frequency of urination, and the passing of membranes in the urine.

Rupture of the cyst into the pelvis or a calyx is followed by the appearance of hooklets and daughter cysts in the urine. The fluid in an intact hydatid is sterile, but should the cyst wall become ruptured, the fluid will make an excellent medium for fl

lowing rupture, therefore, sym

septic poisoning may develop.

following rupture, due to absorption of antigen from the cyst.

Diagnosis. The diagnosis in the open variety is easy because hooklets and daughter cysts can be readily demonstrated in the urine. In the closed variety the diagnosis is very difficult and has rarely been made postoperatively in the cases reported.

Physical examination will usually reveal a mass in the kidney region, and more or less tenderness. Percussion over the mass, if in the lower pole, may elicit the so-called "hydatid thrill"—a fluctuation which is a characteristic of the hydatid.

The pyelogram usually shows some filling defect suggestive of cyst or tumor of the kidney, but is of no assistance in determining the nature of the cyst.

Generalized eosinophilia is present in about one-fourth of the cases, and suggests the possibility of hydatid disease.

Various precipitin, complement-fixation, and intradermal tests have been developed, which have proven to be valuable aids in the diagnosis of the renal type of hydatid disease, although in this country the difficulty of procuring the fresh antigen may frequently prove a barrier to their employment. The precipitin test, improved and simplified by K. D. Fairley (1923) and by Bryce, Kellaway, and Williams (1924), using one-half phenolized hydatid fluid (unheated) and one-half patient's serum, provides a satisfactory specific criterion. The complement-fixation test, first advocated by Weinberg (1909) and modified by N. H. Fairley (1921-22), uses clear, sterile, unpreserved hydatid fluid from human or sheep

cysts as antigen. (This test is positive in over 80 per cent of cases.) The *intradermal test* of Casoni is generally regarded as more sensitive than either of the above, giving over 95 per cent positives. This test was improved by Dew, Kellaway, and Williams in 1925. The injection of 0.2 cc. of sterile, unpreserved hydatid fluid into the skin produces a wheal up to 5 cm. in diameter with pseudopodia in about 20 minutes in all positive cases, with no false positives, and is the test of choice in all except old, complicated cases, when the complement-fixation test should be employed (Craig and Faust).

In one of the two cases seen by us, the diagnosis was easily made as daughter cysts were found in the urine. The patient, a 30-year-old male, had lived on a sheep-raising farm in Sardinia, where there were many dogs. He had had intermittent attacks of pain in the right kidney area for 2½ years, with frequency of urination and the passage of membranes from the urethra during and after the attacks of pain. A firm mass was palpated under the right costal margin. The cyst, which was located in the upper pole, had ruptured into the renal pelvis, making nephrectomy necessary.

Our second patient was a young woman who had recently come from Greece, where she had lived on a dairy farm. She complained of pain in the left flank, associated with frequency of urination of 2 months' duration. A mass, which was apparently connected with the left kidney, was felt in the left upper quadrant. The pyelogram showed an enormously enlarged kidney and an irregular filling defect suggestive of a tumor. At operation, a large cyst of the lower pole was found; this was removed with the kidney, the patient making a rapid recovery.

Prognosis. The outlook for recovery from echinococcus infection of the kidney is good, although it is sometimes necessary to sacrifice the kidney. Frequently, however, conservative surgery suffices.

Treatment. Surgery is the only possible means of relief, but there is some variance of opinion as to the best methods to pursue. In open hydatid cysts of the kidney, nephrectomy is the operation of choice, if the opposite kidney is functionally adequate. Care must be taken not to spill the contents of the cyst. For the closed cysts, various methods have been advocated: nephrostomy through a simple lumbar incision; marsupialization; heminephrectomy; suture without drainage.

Marsupialization consists in making an opening in the cyst wall, through which the contents are evacuated, and then fixing the edges of the cyst wall to the skin edges of the abdominal wound. A rubber drainage tube is left in the sac thus formed.

Suture without drainage, often known as the "Australian method," is carried out by the following steps (Craig and Faust): (1) The adventitia surrounding the cyst is exposed by incision over the most prominent or most dependent part of the tumor. (2) The contents of the cyst are aspirated through a large-caliber needle or trocar connected with a closed suction apparatus; 10 to 50 cc. of 10 per cent formalin solution is then injected, and the fluid slowly withdrawn from the sac, the withdrawal occupying 5 minutes or more. (The formalin causes death of the brood capsules and scolices within a very short time.) (3) The adventitia is incised down to the actual cyst, and the cyst with its contents separated from the adventitia and removed. (4) After swabbing the adventitia with 10 per cent formalin solution and leaving a small amount of the solution in the cyst bed, the cavity is obliterated wherever possible by setting in intracapsular sutures, the adventitia closed with a double row of catgut sutures, and the cavity closed without open drainage, anchoring the adventitia to the tissue beneath the line of incision.

(7) *Bilharziasis of the Kidney*

Infection with *Schistosoma haematobium* is common in the bladder and lower part of the ureter, only occasionally noted in the upper ureter, and decidedly rare in the kidney. Very few cases of renal involvement have been reported in this country, the latest apparently being that of A. R. Stevens (1935), in which the lesions were papillomatous in type and involved the calyces and pelvis, ureter, and adjacent portion of the bladder. Although infection of the renal pelvis from a previously infected bladder or ureter appears to be uncommon, the possibility of such an occurrence is strong enough to merit watchfulness on the part of practitioners under whose care these infrequent bilharzial infections may come. If the ureter—particularly the upper portion—shows the characteristic lesions, the possibility of the kidney being likewise involved should be kept in mind.

Bilharziasis of the urinary tract has been adequately covered in the sections on Diseases of the Bladder (p. 1030) and of the Ureter (p. 1248), to which the reader is referred.

(8) *Actinomycosis of the Kidney*

Incidence. Actinomycosis is a relatively rare disease in this country. Sanford and Voelker's survey of 670 cases in the United States, in 1925, included only 1 case of renal involvement. Clinically, the renal lesions are termed "primary" when no other lesion can be found, and "secondary"

when they are a metastatic or hematogenous infection from a primary lesion in the lungs, liver, intestines, or other organ. Most authors are of the opinion that a truly primary renal infection never occurs. Von Lichtenberg found only 7 reports of so-called primary renal actinomycosis up to 1927. Cumming and Nelson (1929) collected 37 cases of renal infection from the literature, in 11 of which the lesions were primary. Hunt and Mayo (1931) found 11 cases of primary renal lesions and added one of their own. Good, studying 62 cases of abdominal actinomycosis,

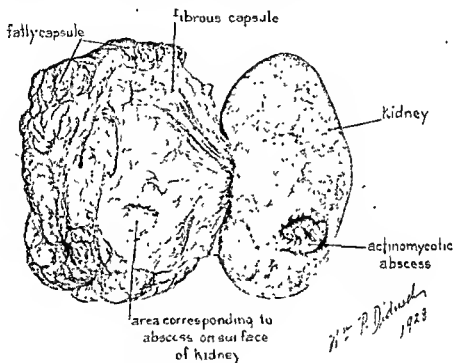


FIG. 320. Actinomycotic abscess involving the left kidney and its capsule. (Christeller.)

found secondary involvement of the kidney in 8 instances. Kretschmer and Hibbs (1936), in a careful perusal of the literature, collected 3 cases of renal involvement in children and added a personal case.

Etiology and Pathogenesis. *Actinomyces bovis*, the causative organism of actinomycosis, is a facultative anaerobe found only in the animal body. It is a branching filamentous organism, which stains by Gram's method. It is fairly easily cultured and is readily killed by heat. The fungus is believed to be a normal inhabitant of the buccal and gastro-

intestinal secretions of man and animals, and in certain instances may penetrate into the tissues, setting up the characteristic lesions of actinomycosis. Numerous reports of the finding of actinomyces in the carious teeth and tonsillar crypts of otherwise healthy individuals—both children and adults—are on record.

Accessory factors favoring the implantation of the fungi into the tissues are trauma, disease, and accompanying organisms. Garceau quotes Wright as surmising that the organism exists in the form of fragmented filaments growing in company with bacteria of the gastrointestinal tract, though he could produce no direct proof of the correctness of this view. Israel believed that "under certain conditions the malignant microorganisms may develop from harmless leptothrix found in the mouth."

It is frequently impossible to demonstrate the portal of entry of the actinomyces. From the primary site the disease extends by continuity of tissue or by the blood stream (rare). Garceau cites the case of Hoover, wherein the disease started in the jaw, reached the lung by invasion of the chest wall, traveled through the lung and perforated the diaphragm, attacked the liver, finding its way through to the lower hepatic surface, and eventually attained the kidney.

The kidney is probably infected most frequently by direct extension of the disease process from a point in the gastrointestinal tract. The disease makes its way through the capsule into the renal parenchyma, finally reaching the renal pelvis, when pus will enter the urine and thus find its way to the bladder. From the alimentary tract the fungus may infiltrate a blood vessel, causing a metastatic lesion to be produced within the kidney parenchyma, whence the process spreads outward to involve the renal capsule, the perirenal tissues, and, in most cases, the ureter. A unilateral actinomycotic process in the lower lobe of a lung may involve the kidney by direct extension through or behind the diaphragm.

Pathology. When the fungi have established themselves in the tissues, they set up a chronic suppurative process, with necrosis and the formation of granulation and connective tissue. The individual lesion appears as a collection of sulphur-yellow granules or linear streaks within the suppurative process. These characteristic granules consist of felted masses of the mycelia of the actinomyces. The abscesses containing the organism are usually multiple and are surrounded by a zone of granulation or connective tissue. Extension usually takes place, as previously

noted, by continuity, with the production of densely indurated lesions which have a tendency to break down and form communicating channels and discharging sinuses.

When the kidney has been invaded by continuity, adhesions will be found between it and the infected adjacent structures; and if an abscess cavity has formed by dissolution of the tissues of the neighboring organs, there may be a sinus to the external surface, through which pus, mixed with yellow granules, will be discharged. The renal capsule will be thickened and eroded, and the parenchyma the site of the characteristic lesions, which, in the kidney, resemble caseocavernous tuberculosis.

Amyloid infiltration may occur with long-continued renal actinomycosis. It is usually bilateral. Frequently, amyloid disease of the kidney will be found when actinomycosis is present elsewhere in the body but there is no evidence of renal invasion. Secondary nephritis and fatty degeneration also occur in connection with renal actinomycosis.

Symptoms and Diagnosis. There is no definite symptomatology. If the kidney involvement is a part of a generalized actinomycosis, the symptoms will be those of a severe sepsis, and any localizing signs or symptoms are likely to be overshadowed by the systemic manifestations, so that the renal invasion may be entirely overlooked.

In the so-called primary type, the disease is likely to be diagnosed as tuberculosis or renal tumor. Pyelography has been of little value. Most diagnoses have been made by pathological studies.

Men are much more frequently affected by actinomycosis than women. No age is exempt.

The most common symptoms are fever, loss of weight, and pain in the kidney area. The persistence of a sinus following nephrectomy for a chronic suppurative process in the kidney, in which tuberculosis has been ruled out, or the formation of a spontaneous fistula, should lead one to suspect the possibility of actinomycosis.

The preoperative diagnosis must rest upon the demonstration of the fungus in the urine or in the pus from a discharging sinus. A history of preexisting actinomycosis elsewhere in the body is, of course, very suggestive.

Prognosis. The prognosis, in general, is poor. The mortality of abdominal actinomycosis is very high, and secondary involvement of the kidney usually occurs late in the course of the disease. In the relatively few cases where the disease is apparently confined to the kidney, nephrectomy offers a good chance of recovery. However, it is very difficult to

discover the exact extent of the disease, and reappearance of the infection elsewhere in the body at a later date not infrequently occurs.

Treatment. In unilateral renal actinomycosis, nephrectomy is the treatment of choice, if there are no extensive lesions elsewhere in the body and if the opposite kidney is capable of carrying on the function of both sides. A number of cures have been reported in these primary cases. If the disease is widespread when the renal involvement is first recognized, nephrectomy will be of little value and the wisdom of performing it is questionable.

Several treatments of the postoperative wound have been suggested, such as leaving the wound wide open, packing it with iodoform gauze, irrigating it with a 2 per cent solution of copper sulphate, etc. Most authors advocate the postoperative administration of roentgen rays over the entire area and of potassium iodide orally or sodium iodide intravenously.

Renal Leukoplakia

Leukoplakia of the renal pelvis must be reckoned a rare lesion, although Kutzmann was able to collect 67 cases from European and American literature in 1929 and several have since been added.

Etiology. The etiology of leukoplakia is not clear. It is suspected—as in the case of cancer—that chronic irritation may have a strong influence on its production (Leukoplakia of the Bladder, p. 1019). Just what irritating influence might act to induce its appearance within the kidney pelvis is merely a matter of conjecture.

Pathology. The lesion is epidermoid in character, being a thickening or keratinization of the epithelium of the renal pelvis. On section of an affected kidney, well-defined membranes will be observed, appearing like patches of silvery-gray skin lying in wrinkles. Sometimes these patches are so tough and leathery that it will be found difficult to lift them from the surface to which they are adherent. When finally they are removed, the underlying tissues will display a papillary surface. The entire interior of the renal pelvis may be lined with this membrane, or there may be only scattered patches interspersed with normal-appearing epithelium. Microscopically the patches have somewhat the aspect of normal cuticle, retaining the skin's characteristic stratified appearance, but a more or less extensive leukocytic infiltration will usually be found beneath them.

Leukoplakia is regarded by many observers as precancerous in nature.

In the urinary tract, squamous-cell carcinoma is known to have developed on the site previously occupied by a patch of leukoplakia in numerous instances. Patch, in a study of 152 cases of squamous-cell carcinoma of the kidney and bladder, found leukoplakia in association with the malignancy in 13 cases. Taylor, commenting on the estimate of Potts that squamous-cell carcinoma follows leukoplakia of the urinary tract in 8.4 per cent of cases, says: "We suspect that this percentage is too low, as it is possible that the leukoplakia occurs more frequently than reported in malignancies of the bladder and kidneys because, as a precancerous lesion, it may be overlooked or entirely replaced, while the malignant tendencies of a leukoplakia may be overlooked, due to insufficient examination of the specimen."

Symptoms and Diagnosis. The symptoms are those of a chronic renal infection or of urinary calculus, and in no way suggest the true nature of the lesion. Clinically, leukoplakia is most likely to be confused with renal tuberculosis. Most tubercular patients, however, are between 20 and 35 years of age, whereas renal leukoplakia is usually seen in the middle-aged and elderly. If obstruction of the ureter by desquamated epithelium occurs, there may be severe pain, but this cannot be distinguished from ureteral colic due to other causes, such as stone or stricture.

Positive identification is possible only at operation or autopsy.

Treatment. The treatment is that of chronic renal infection, because the lesions cannot be positively diagnosed except by bisection of the kidney. Most urologists advise nephrectomy for a unilateral lesion, because of the supposedly precancerous nature of the disease.

Cysts of the Kidney

Renal cysts may be divided into *polycystic* and *simple*. Polycystic disease is a congenital condition, but because clinical manifestations often do not appear until adult life, and are likely to be confused with those of acquired diseases of the kidneys, it seems advisable to consider the subject here rather than with congenital anomalies. Simple cysts are acquired. They may be subdivided into *unilocular cysts* and *multilocular cysts*. Other forms of acquired cyst are *hydatid cyst*, caused by *Taenia echinococcus* (Echinococcus Disease of the Kidney, p. 1520) and the *small, multiple retention cysts* associated with chronic nephritis or infection. The latter have slight clinical or surgical importance, being usually discovered only on exposure of the kidney.

Renal cysts were described more than 300 years ago by Fabricius de

Hilden, who died in 1624, but no clear-cut classification of the various types was made until 1876, when Laveran distinguished between simple cysts and polycystic disease. The first review of the literature and citation of cases of renal cysts was that of Lejars (1888). Although cysts of the kidney are relatively rare, the literature is voluminous.

POLYCYSTIC DISEASE

Polycystic disease of the kidneys is an extensive invasion of the renal parenchyma by cystic formations which are almost surely of congenital origin. The disease is apparently unrelated to other cystic conditions of the kidney. In advanced cases the entire kidney is a mass of cysts varying from small vesicles to cysts 6 or 7 cm. in diameter.

The condition appears to be bilateral from the outset, although the process is likely to be more advanced on one side than on the other. Advanced instances of the disease are found at birth, as well as in extreme old age. In the fetus, the polycystic kidneys may be so large as to impede delivery of the child. Such infants die *in utero* or shortly after delivery. If the condition is compatible with life, it generally remains undetected until adulthood; or, as postmortem examinations have repeatedly shown, it may not be suspected in life, death being due to other causes, while the kidneys have functioned satisfactorily.

Incidence. Polycystic disease of the kidneys is uncommon, but occurs often enough to be of considerable clinical importance. The following statistics give some idea of its incidence. Of 389,773 patients treated at the London Hospital from 1900 to 1924, only 79 had clinically manifested polycystic kidneys (Cairns). Naumann (cited by Dunger, 1904) found only 16 cases of polycystic disease in the records of 10,000 necropsies. Davis (1925) states that the combined statistics of Barnett, Preitz, and Garceau, from 23,190 autopsies, revealed 67 cases. At the Mayo Clinic, 9 cases were found in 9,171 necropsies; clinically there were 193 cases in 680,000 registrations (Braasch and Schnacht, 1933). Oppenheimer (1934) gives the incidence at the Jewish Hospital, Brooklyn, as 13 cases in 2,060 autopsies. At Mount Sinai Hospital, New York, there were 60 cases in 220,000 admissions; 14 cases were seen in 6,000 necropsies. Bell (1935) found 44 cases in 22,393 autopsy records of the University of Minnesota Hospital. He mentions that the incidence in any series is greatly influenced by whether or not still-births and the deaths of very young infants are included in the figures. Analysis of the records of his hospital showed 8 instances of polycystic disease in

1819 still-births, with 6 cases in infants under 6 months of age. At the Brady Foundation, in the New York Hospital, 30 cases of polycystic kidneys have been clinically diagnosed in the 19 years between 1924 and 1943.

Familial Occurrence. The hereditary aspect of polycystic kidneys has been so frequently demonstrated that a familial history is now considered of the greatest diagnostic value.

Cairns, in 1925, published a study of three generations of a family of 42 individuals, 8 of whom had polycystic kidneys, while 2 members, who were then children, had palpable kidneys which were probably cystic. He found in the literature but one record of polycystic disease in three generations of a single family; this was a Swedish family, the history of which was first recorded by Bull (1910) and later continued by Paus (1914). In 1928, Cumming made public another instance of 10 cases of polycystic kidneys in three generations of the same family. There have been numerous reports of inheritance by a child from a parent (two generations); and instances where a number of members of a single generation presented the anomaly are common.

It is our practice, when we discover polycystic kidneys in one member of a family, to send for the others, and, if investigation reveals the condition, impress upon the afflicted individual the importance of remaining under observation.

Etiology. Polycystic disease of the kidneys has long been recognized as being of congenital origin, due partly to the finding of several cases of the disease in one family, and partly to the frequency with which such kidneys are found in fetuses and the newborn. However, the pathogenesis, though productive of a host of theories, is still in doubt.

For many years, Virchow's theory that the cysts are due to papillitis, with occlusion of the papillary ducts, was commonly accepted, but was abandoned when it was demonstrated that obstruction of the ducts led to atrophy, rather than cystic changes, of the ducts.

Hildebrandt's theory that the cysts are due to defective union of ureteral and metanephrogenic fundaments during development is based on the knowledge that the straight collecting tubules and the renal pelvis take their origin in the ureteric bud of the wolffian duct, later uniting with the convoluted tubules, which arise from a separate embryological structure, the metanephrogenic blastema. He argues that failure of union between the convoluted tubules and the collecting tubules would produce multiple cysts at the time secretory activity of the kidney

should normally begin. Later investigators have found direct continuity between cysts and collecting tubules, proving that retention alone cannot account for cyst-formation.

Hepler, basing his belief on the work of Hinman and Morison upon the renal circulation, showed that mere occlusion will not cause cyst-forma-

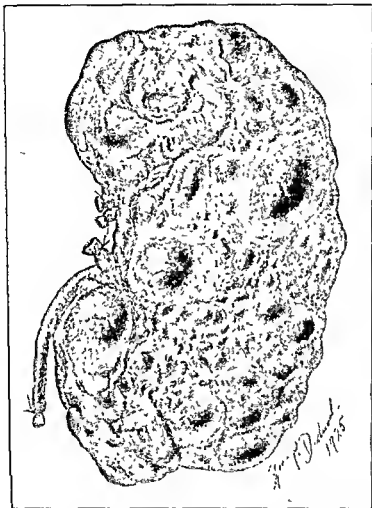


FIG. 321. External view of polycystic kidney. Autopsy specimen.

tion, but when interference with the local blood supply takes place, cyst-formation promptly follows. Hepler's work was done in an investigation of solitary cysts, but his conclusions are applicable to all types of true cyst arising in the kidney.

Davis' view that polycystic kidneys in man result from partial cessa-

tion of development at the mesonephric stage, with later degenerative changes, finds backing in comparative anatomy. In those lower forms of animal life where the normal adult kidney is of the mesonephric type, renal similarities to the human polycystic organs are to be recognized.

Kampmeier's theory that the cysts arise from persistence of primitive renal tubules has been demonstrated, at least in part, in fetal kidneys. The ureteric bud, developing as the *nephrogenic cap*, is first in conjunction with primitive tubules which never reach the stage where their lumina become continuous with the lumen of the primitive renal pelvis. After these tubules degenerate, the pelvis begins to send out branches which do become continuous with a new set of renal tubules that replace the primitive group. These tubules eventually degenerate and completely separate from the pelvis before they entirely disappear. They remain long enough, however, to constitute a makeshift kidney. The beginnings of the permanent kidney are laid when a third set of tubules arises and is united with the primitive ureter. According to Kampmeier, the tubules of the second series, once separated from the primitive pelvis, may not immediately disappear, but remain to become dilated to many times their original dimensions, thus forming cysts. Extensive observation on fetuses of many different stages of development convinced this investigator that abnormal development of the provisional tubules is responsible for this anomaly as generally encountered.

Pathology. In well-advanced polycystic disease, the kidney will have the appearance of being changed to a mass of cysts of varying sizes, some of which have almost transparent walls through which the contained fluid is plainly visible. The surface contour is irregular, due to the underlying cysts, but the characteristic kidney outline will usually be discernible.

The kidney may reach an enormous size. The congenital cystic kidneys sometimes seen during labor may be so large as practically to fill the abdomen. The adult type does not often attain sufficient size to be detectible by inspection, although an occasional case has been reported wherein the kidney formed an easily recognizable mass, visible as well as palpable. Very often the disease, and hence the size of the kidney, will be more marked on one side than on the other.

On section, the cysts are seen to be scattered throughout the renal parenchyma. They do not communicate with each other or with the renal pelvis, though occasionally a cyst may rupture into the pelvis. In advanced cases the renal tissue is reduced to a minimum, and occurs as thin strips of cortical substance lying between the cysts and showing the changes of pressure atrophy and interstitial fibrosis.

The cysts often contain a clear, yellowish fluid, but the contents vary considerably. The fluid in practically all polycystic kidneys of adult life contains blood and pus, evidence of hemorrhage and infection. The cystic contents have been variously reported to contain calcium oxalate, uric acid, cholesterol, leucin, cystine, fat, blood, and pus.

The fact that it is increase in the size of the cysts, rather than increase in their number, which causes enlargement of the kidney, has been commented on by Belt, as follows:

Although the stages have not been identified, it is highly probable that polycystic kidneys at birth have a still greater proportion of intact parenchyma than is found in the subclinical group at postmortem. In childhood and youth the persistent islands of parenchyma hypertrophy and compensate for the tissue destroyed by the cysts. This is probably the reason why there are so few deaths between infancy and the third decade. But in adult life the ability to hypertrophy is greatly decreased, parenchyma is destroyed more rapidly than it can be replaced, and the patient progresses toward renal insufficiency. The destruction of parenchyma is largely due to the cysts. . . . The destructive effects of pressure are easily observed between and around the cysts. The tortuous thick-walled arteries and the elevated blood pressure probably contribute to some extent to the destruction of the parenchyma. The expansion of the cysts produces a pressure atrophy of the tubules and glomeruli. The abundant interstitial tissue, especially in the medulla, becomes more dense and fibrous with age, and also compresses the tubules. Some of the smaller cysts in adult kidneys represent hypertrophy of persistent tubules, or they may be tubules that originally communicated with the pelvis which were later obstructed by the pressure of connective tissue or cysts. The great majority of the larger cysts are probably of fetal origin.

Polycystic disease is believed to be always bilateral, even though inspection at the time of operation may sometimes show one grossly normal kidney. In many instances, advanced cystic degeneration has been found on one side and a macroscopically normal kidney on the other, yet microscopic examination invariably has revealed unmistakable evidence of early cysts in the apparently healthy organ.

Other anomalies are commonly associated with that of the kidney, especially the tendency to deformity in the skeleton, and cystic conditions of the liver, ovary, uterus, epididymis, and spleen.

Symptoms and Signs. In the adult, the chief symptoms and signs are renal insufficiency, lumbar pain, hematuria, albuminuria, and a palpable tumor in one or both loins. Nephritic manifestations, such as nausea, vertigo, anorexia, headache, lassitude, and loss of weight, are common. Polycystic kidneys show a marked tendency to hemorrhage and infection. Hematuria is frequently the symptom which impels these patients to seek medical advice. This may be slight or marked,

but is usually *intermittent*, of long duration, and painless. In other cases, pyuria or lumbar pain may be the chief complaint. Any other form of renal disease may be engrafted upon the congenitally cystic kidney, in which event the symptomatology of the complication will be present. Again, urological symptoms may be lacking and the clinical manifestations those of a gradually developing chronic glomerulonephritis, which may continue for years, with renal dysfunction, uremia, anuria, and finally death.

Diagnosis. Polycystic disease is observed in early infancy and in adult life (usually after the twenty-fifth year), with a period during childhood and youth when very few cases are seen. Of the 44 patients reported on by Bell, only 1 was between the ages of 4 months and 25 years. One of our patients was a 9-year-old boy. All the infants die shortly after birth.

Because of the tendency of the disease to be hereditary, complete and accurate investigation of the patient's family history is of great importance.

The diagnosis is based on the symptoms noted above, the physical findings, and the appearance of the pyelogram. The urinary findings resemble those of interstitial nephritis, and are not of themselves characteristic. Excretion tests may at first be quite normal, but in the later stages may indicate advanced or complete destruction.

Lowered renal function, or blood in the urine, and a palpable mass in both loins should suggest the possibility of polycystic disease. Occasionally one may even feel the irregularity of the kidney's surface caused by the presence of the cysts. Often, however, only one kidney, or neither organ, is palpable.

Urography, either intravenous or instrumental, will give definite diagnostic information in most cases (Roentgenography of the Genito-Urinary Tract, p. 159). In advanced cases the pyelogram often simulates renal neoplasm. The bilateral nature of the deformity in polycystic disease is an aid in differentiation. The appearance of the pyelogram will vary with the stage of the disease; and there may be considerable difference in the extent of the deformities in the two kidneys of the same patient. The changes affect the calyces chiefly, and consist of alterations due to compression of the calyces by the cysts. In the earlier stages they consist mainly in a crescentic distortion of the terminations of the minor calyces. Later there is elongation of the major calyces and infundibula, with widening of the minor calyces. The indentation of the enlarged

cysts can sometimes be made out. One or more of the minor calyces may be entirely obliterated. As a rule, the narrowed pelvis and elongated calyces extend over a space larger than the usual kidney area.

It is our practice to do only intravenous urography once the diagnosis has been confirmed, because we feel that ureteral catheterization constitutes a very definite hazard in these cases, even though no urinary infection is demonstrable. Should retrograde pyelography be deemed necessary, it must be done with marked regard as to gentleness and asepsis.

Prognosis. The prognosis is poor, although under certain circumstances patients are sometimes enabled to live to a good age and in comparative comfort. Patients afflicted with this disease are liable to renal infection and become exhausted easily. Unless they live, very carefully, they are subject to many calamities. When operation is necessary, the polycystic kidney patient is not a good risk, and, if one kidney is removed, is not likely to survive for more than a year or two, although survival for much longer periods has been reported in a number of instances.

Treatment. In general, the treatment of polycystic disease is medical. Due to the bilateral and progressive nature of this disease, surgical intervention is contraindicated except in imperative circumstances.

Even though the disease is progressive in nature, careful medical management will do much to prolong and make more comfortable the lives of these patients. The destruction of renal tissue, unless hastened by infection, urinary back pressure, or stone-formation, often proceeds very slowly. The avoidance of infection is, therefore, of supreme importance.

These patients require plenty of rest, and must do everything in moderation. They should avoid extremes in temperature, particularly cold, and, whenever possible, should live where the winters are mild. Sufficient fluids, and a low-protein diet to reduce the work of the impaired kidneys, are recommended. Adequate drainage may be maintained, and acute symptoms relieved, by occasional careful dilatation of the ureters and renal pelvic lavage. Repeated and regular examinations are important.

Severe hemorrhage, gross infection, serious obstruction, tuberculosis, tumor, stone, or rupture may demand surgical intervention (Operative Treatment of Renal Cysts: Polycystic Disease, p. 1686). Operative maneuvers require the utmost care and good judgment, and assurance of a sufficient functional reserve in the opposite kidney is even more important than in the case of congenitally normal kidneys.

SIMPLE CYSTS OF THE KIDNEY

(1) UNILOCULAR CYSTS

Simple unilocular cysts of the kidney are usually of large size and unilateral, and occur in adult life. While generally solitary, several of them not infrequently occur in the same kidney simultaneously. They are of two types: *serous* and *hemorrhagic*. They are to be distinguished from multilocular and hydatid cysts, the retention cysts of nephritis and hydronephrosis, and from polycystic disease.

Incidence: Age: Sex. Large simple cysts of the kidney, while uncommon, are not as rare as we have been led to believe. Young in his *Urology*, states that no case of solitary cyst had been found in 12,500 urological cases in the Brady Institute up to 1926. On the other hand, 32 cases were observed between 1928 and 1938 in a group of 11,879 urological cases at the Squier Urological Clinic of the Presbyterian Hospital, New York (G. W. Fish, 1939). At the Brady Foundation, in the New York Hospital, we have clinically observed 18 cases of simple cysts between the years 1921 and 1943, in 4 of which more than one cyst was present in the affected kidney. Hepler, in 1930, collected 249 cases from the literature (212 serous and 37 hemorrhagic), to which he added 7 cases (4 serous and 3 hemorrhagic) from his personal experience. The cases reported since bring the total over 300.

Simple cysts of the kidney are discovered most frequently in the fourth and fifth decades of life. Very few cases have been found in children. The condition has been slightly more common in females than in males in most of the reported series.

Etiology. The etiology of *simple serous cysts* of the kidney is indefinite. Outstanding among the current theories are the following:

1. The cysts are congenital in origin, and due to the persistence and dilatation of primitive renal tubules, as already mentioned in connection with the etiology of polycystic kidney (Kampmeier).

2. They have their origin in embryonal rests (Latteri).

3. They result from tubular obstruction together with interference with the local blood supply (Hepler).

4. They are retention cysts, due to some obstruction in the uriniferous tubules with continued secretion of urine. Localized inflammation is the most frequent cause of such obstructions.

Supporters of the congenital theory contend that the cysts are slow-

growing and do not reach sufficient size to produce noticeable symptoms until relatively late in life. However, the fact that Hepler produced solitary cysts experimentally by a localized arterial block and tubular obstruction, as well as the age incidence of 40 years or over, the rarity in children at autopsy, and the relative frequency of a history of sudden onset of symptoms and comparative rapidity of growth of the tumor,

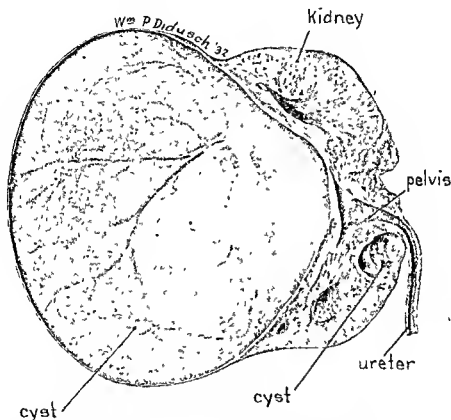


FIG. 322. Large simple cyst of the right kidney. View on section. The cyst did not communicate with the renal pelvis. Note smaller cyst near the hilum of the kidney.

favor an acquired origin. "It would seem more reasonable," states Hepler, "to suppose that they were related in some way to the acquired renal lesions which are more common in middle life."

Regarding the theory that the cysts are retention cysts, due to obstruction of the tubules, there are certain discrepancies which make this supposition more or less untenable, namely: (1) There is no evidence of

such obstruction in many cases; (2) pathological lesions so situated as to block large groups of tubules are comparatively common, yet solitary cysts are rare; (3) obstruction to the tubules at the papilla has been experimentally induced and, although there was dilatation, which persisted in some cases, the experimenters did not succeed in producing any cysts.

The rare *hemorrhagic cysts* of the kidney are generally believed to originate as simple serous cysts, which later are the site of hemorrhage of unknown cause. By the time the cyst is discovered, there is no way of determining whether it began as a simple serous cyst or whether it contained blood from the outset. Other current etiological theories are that such cysts are an unusual type of hematoma; that they are of an aneurysmal nature; that they are due to embolic or thrombotic infarction. The factor of trauma must also be considered.

Pathology. Simple cysts, in contradistinction to polycystic disease, are usually unilateral, though bilateral occurrence is occasionally encountered. The latter, however, is rare. There is apparently no predilection for either side, the right and left sides being involved about equally.

The cyst may be situated in any portion of the kidney. The predominant location is the lower pole, but a goodly number are found in the upper pole, and a few, like the large calcified cyst reported by Kirwin in 1926, are found in the medial portion. Although the terms "simple cyst" and "solitary cyst" are often used interchangeably, actually these cysts are by no means invariably solitary; there may be two, three, or even more of them, though one is always much larger than the others. When multiple large cysts are present, some may be unilocular and others multilocular. Serous and hemorrhagic simple cysts may also occur in the same kidney, a fact which, in the opinion of some writers, favors the theory that the latter begin as serous cysts. Multiple large cysts must be differentiated from polycystic disease.

Simple cysts vary considerably in size and may reach enormous dimensions. Of 32 large solitary cysts reported by G. W. Fish, the largest contained 10 liters and the smallest approximately 350 cc. In our series, the largest cyst was 40 cm. in diameter.

The exact part of the renal parenchyma from which a given cyst has arisen is very difficult to discover at the advanced stage of development at which most renal cysts are first observed; hence there is some difference of opinion as to whether the cortical or the medullary substance most

often gives rise to cyst-formation. It is now generally believed, however, that the cyst usually arises in the cortex near the surface, and has no communication with the pelvis.

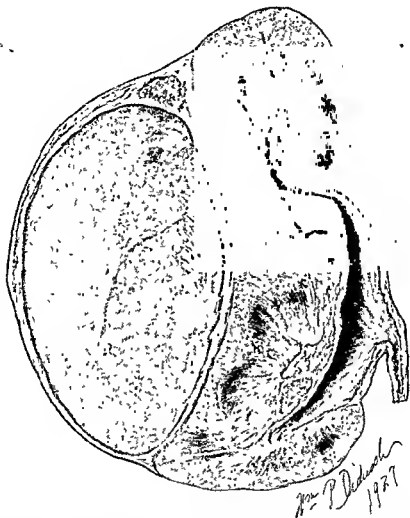


FIG. 323. Calcified solitary cyst of the kidney. Sectional view. The cyst arises from the medial portion of the kidney, and has no communication with the renal pelvis. Male, aged 43 years. (Kirwin's case.)

The cyst is usually densely adherent to the renal parenchyma. The cyst wall is composed of fibrous tissue poorly supplied with blood vessels, and is sometimes thin, again indurated and thickened, and occasionally calcified. Ordinarily the internal surface is smooth and regular, but occasionally there are grooves and furrows and incomplete septa, sug-

gesting the multiple origin of what appears as a single, unilocular cyst. As a rule, the cyst is partly lined with epithelium of a flat or cuboidal type, but evidence of an epithelial lining may be entirely lacking. The renal tissue in contact with the cyst wall usually shows atrophic changes.

The content of the cyst, if uncomplicated by infection or hemorrhage, is a clear, yellowish, watery fluid containing albumin, chlorides, phosphates, cholestrin crystals, epithelial cells, a few leukocytes, and, occasionally, traces of urea.



FIG. 324. Calcified solitary cyst. The pyelogram shows the cyst held in the grasp of the renal pelvis. Note ptosis of the kidney and kinking of the ureter, due, probably, to the weight of the cyst. (Kirwin's case)

Hemorrhagic cysts contain bloody fluid or clotted blood. These hemorrhagic cysts are frequently malignant (13 out of 42 cases, Whitmore, 1936). LeComte is of the opinion that if careful examination were to be made, an even larger proportion of hemorrhagic cysts would be found to contain malignant elements in their walls. When malignancy is present, it is most commonly found in the portion of the cyst wall adjacent to the renal parenchyma. Carcinoma, hypernephroma, and sarcoma have all been observed.

Symptoms and Signs. The nature and severity of the symptoms depend on the size and location of the cyst (or cysts), and whether the cyst communicates with the calyces or renal pelvis. Cysts of moderate size

may cause no symptoms whatsoever, and may be discovered only at operation for some other disorder—usually hydronephrosis, calculus, or infection—or at autopsy. Usually, however, when the cyst has attained considerable size, it gives some indication of its presence, though this is often so indefinite as to be of little diagnostic aid. Frequently patients give a history of vague symptoms which have been present for a long period of time, sometimes years. In other cases, the symptoms were first in evidence after some unusual physical effort or strain.

The predominant symptoms are pain or discomfort on the affected side, and gastrointestinal disturbances of varying degrees, due to pressure of the cyst on the intra-abdominal organs. The pain varies in character, being at times merely a sense of intra-abdominal weight, and in other cases a vague discomfort or definite pain in the loin of the affected side. In such cases the patient himself may note a mass in the abdomen, or examination may reveal a palpable tumor. Often, however, no tumor can be palpated. Large cysts occurring at the upper pole may cause pressure on the diaphragm, thus producing cough, dyspnea, and pain in the shoulder on the affected side.

Hematuria may be present in some cases. Relative function tests may show unilateral reduction, but frequently only a small portion of the kidney parenchyma is involved and, unless there is coexisting disease, no effect on the phenolsulphonphthalein output will be observed.

Diagnosis. Simple cysts of the kidney are not likely to be suspected and searched for unless they are large enough to produce a palpable mass, or to pull on the kidney and produce lumbar pain. They are frequently found during exploratory operation for suspected neoplasm, or are an incidental discovery in operations for hydronephrosis, stone, or infection.

Preoperative diagnosis is difficult and is largely based on the roentgenographic and pyelographic appearance of the affected kidney. In unusual cases the mass may be palpated in the loin. It is often impossible to differentiate clinically between cyst and neoplasm.

The plain x-ray film frequently shows the outline of the cyst, which usually appears as a smooth, globular shadow at the bottom, top, or center of the kidney; this, as a rule, is less dense than the shadow of the kidney itself. In cystic tumors, the outline of the kidney or psoas muscle, or both, will be recorded on the x-ray film through the shadow of the cyst, which is of lesser density; whereas solid tumors, due to their density, may completely obliterate these shadows if they overlie them (Ullman Reaves, 1938).

The pyelogram may be normal; or it may show some evidence of

pressure or pulling on the pelvis or calyces, together with distortion of the ureter and a change in the position and axis of the kidney as a result of the weight of the mass. There may be calyceal changes in the form of clubbing or crescentic deformity; or encroachment of the cyst may result in compression and flattening of the adjacent portion of the renal pelvis and calyces with, sometimes, dilatation above the compressed portion.

Conditions from which cyst of the kidney must be differentiated are renal neoplasm, hydronephrosis, gall-bladder disease, cysts of the liver, spleen, and pancreas, ovarian tumors, and other tumors of the adjacent organs. A cyst may be differentiated from a large hydronephrosis by the absence of pyelectasis and of urinary retention, and by the relation of the shadow of the cyst to the pyelogram and to the ureter.

Prognosis. The prognosis, unlike that of polycystic disease, is good. Since these cysts tend to grow out from, rather than into, the kidney substance, destruction of the renal parenchyma by compression occurs only in the area immediately adjacent to the cyst, and usually is minimal. Conservative surgery, therefore, frequently suffices.

Treatment. Operation is the treatment of choice except when contraindicated by associated disease making surgery inadvisable (*Operative Treatment of Renal Cysts*, p. 1688). Aspiration through the loin, followed by the instillation of a sclerosing material, such as 50 per cent dextrose, gives good results when operation is not deemed advisable, and the danger of spreading a malignant process or producing infection is negligible (G. W. Fish, 1939).

(2) MULTILOCULAR RENAL CYSTS

Multilocular renal cysts are apparently very rare. Meland and Braasch, reporting 6 cases from the Mayo Clinic in 1933, were able to find only 4 previous reports.

Etiology. The same factors which probably operate to produce most unilocular simple renal cysts—namely, localized interference with the blood supply, together with tubular obstruction—are responsible for the development of multilocular cysts. In the former, however, there is at the beginning a single cavity; whereas, in a multilocular cyst, several cavities arise at the beginning and subsequently enlarge and join together to form a many-chambered cyst. The fact that some unilocular cysts show incomplete septa suggests that they have formed by the fusion of the walls of a number of smaller cysts. Had such fusion of the individual walls failed to take place, a multilocular cyst would have formed.

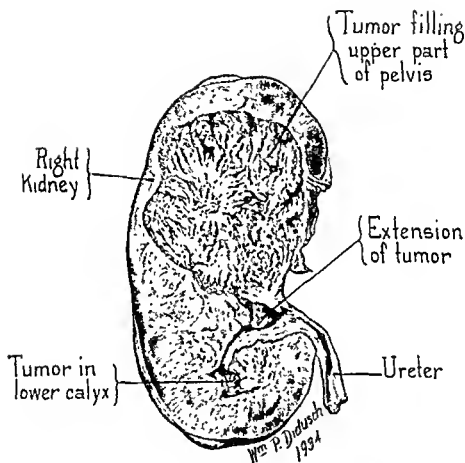


FIG. 325. Papillary carcinoma completely filling the upper part of the renal pelvis, with extension of the tumor to the ureteropelvic junction and the lower calyx. Sectional view of operative specimen

Pathology. Multilocular cysts, like unilocular simple cysts, are almost always unilateral and involve a localized area of the kidney, most commonly the lower pole. The cyst may contain only 3 or 4 chambers, or as many as 30 or more. The dividing walls are entire. Microscopically, the walls of multilocular and unilocular cysts are similar. Serous and hemorrhagic types may occur.

Symptoms: Diagnosis: Prognosis. What has been said above regarding the symptoms, signs, diagnosis, and prognosis of solitary cysts applies also to the multilocular type. Symptoms and signs are produced because of the size and position of the cyst.

The main point in diagnosis is to differentiate multilocular cystic kidney from congenital polycystic disease. Their only point of similarity is the multiplicity of cystic cavities. Polycystic disease is bilateral and diffuse, while multilocular cysts are unilateral and localized. Multilocular cysts produce only pressure symptoms, while polycystic disease produces renal insufficiency, tumor, and, frequently, hematuria.

Treatment. The treatment is surgical, and similar to that of unilocular cysts (Operative Treatment of Renal Cysts, p. 1688).

Tumors of the Renal Pelvis and Kidney

There are numerous definite varieties of tumors involving the kidney, depending upon their origin. By far the most common tumors in adults are the carcinomas of the renal parenchyma, particularly the large, clear-celled adenocarcinomas commonly referred to as "hypernephromas." Much less often, in adults, one sees papillary tumors arising from the mucosa of the pelvis and calyces. In children, the clinically important tumor is the embryonal mixed growth usually called Wilms' tumor.

For the sake of convenience, we will consider renal tumors under three major heads: (1) tumors of the renal pelvis, (2) tumors of the renal parenchyma in children, (3) tumors of the renal parenchyma in adults.

(1) Tumors of the Renal Pelvis

Tumors arising in the renal pelvis and calyces constitute an entirely different group from those having their origin in the parenchyma. They may be benign or malignant, and pathologically are akin to tumors arising in the vesical and ureteral mucosa. The majority are epithelial, about 75 per cent being of the papillary variety.

Incidence. Primary tumors of the renal pelvis are rare in comparison with those arising in the parenchyma of the kidney. Judd (1919) found

only 3 primary tumors of the pelvis in 207 cases of kidney tumors at the Mayo Clinic; Israel and Israel found 6 pelvic tumors among 126 cases of renal neoplasm; MacKenzie and Ratner (1932) estimated that only 5 to 7 per cent of all renal tumors occur primarily in the pelvis. Of 318 nephrectomies for renal tumor reported by Hunt in 1927, 23 were for primary epithelioma of the pelvis; of 55 nephrectomies for renal tumor reported by Thomson-Walker in 1929, 10 were for pelvic tumors.

Most of the tumors occur in individuals between the ages of 40 and 65 years, although pelvic tumors have been seen in the very young and the very aged. The papillary growths are found more often in men than in women; the squamous-cell tumors about equally in both sexes. The right side appears to be affected slightly more often than the left.

Etiology. The origin of tumors of the renal pelvis is still uncertain. Non-papillary pelvic neoplasms are frequently associated with renal stone (11 of 43 cases, Kretschmer; 5 of 18 cases, Cabot). With the papillary growths, associated calculous disease is less common. Chronic irritation and infection, by producing leukoplakial changes and other forms of metaplasia of tissue, probably play a prominent part in the causation of the squamous-cell type of carcinoma. The rare mixed tumors are undoubtedly embryonic in origin.

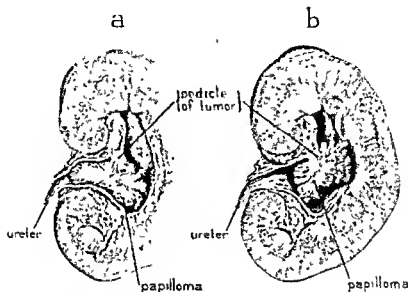
Pathology. The vast majority of tumors of the renal pelvis arise from the mucous membrane lining the pelvis and calyces. Tumors of connective tissue or of embryonal origin, such as sarcoma, myxoma, angioma, and mixed tumors, have been reported, but are very rare.

Renal pelvic tumors may be divided into the following:

- | | | |
|---------------------------------------|---|---|
| 1. Papilloma (benign) | } | Epithelial tumors (papillary) |
| 2. Papillary epithelioma | | |
| 3. Papillary carcinoma (infiltration) | | |
| 4. Alveolar or scirrhous carcinoma | } | Epithelial tumors
(non-papillary) |
| 5. Squamous-cell carcinoma | | |
| 6. Sarcoma | } | Connective tissue and embryonal
tumors (very rare) |
| 7. Rhabdomyoma | | |
| 8. Myxoma | | |
| 9. Angioma | | |
| 10. Fibroma | | |
| 11. Mixed types | | |

Papillary Tumors. Pathologically, the papillary tumors of the renal pelvis, like the familiar papillary neoplasms of the bladder, are (1) the papilloma, (2) the papillary epithelioma, and (3) the papillary carcinoma.

The *papilloma* is usually multiple, appearing as a villous growth which is very vascular and bleeds easily. The growths may involve only a small area, or be extensively distributed over the mucosa of the pelvis and ureter, and even of the bladder. Microscopically, the papilloma consists of branching clusters of stroma, composed of minute blood vessels, covered with many layers of transitional epithelium. The tumor cells are cuboidal, cylindrical, or elongated, and round-cell infiltration is



Wm P Didusch 1930

FIG 326. Papillary carcinoma of the renal pelvis. Operative specimen, view on section. (a) Shows the tumor obstructing the pelvis (b) Shows the movability of the tumor, which is attached to the pelvic wall by a narrow pedicle.

present. The structure is typical and uniform. Though usually benign, the papilloma has a tendency to become malignant.

The *papillary epithelioma* appears as a villous or warty, ramifying out-growth from the pelvic mucosa. It is more compact than the simple papilloma, and early shows a tendency to invade the submucosa. Areas of ulceration are often visible. Infiltration of the connective tissue indicates a true *papillary carcinoma*. Hematuria is an early symptom of most of these growths, because they are highly vascular, consisting almost wholly of thin-walled blood vessels held together by transitional epithelium, with, at times, a solid growth beneath this feathery exterior.

Differentiation between benign and malignant tumors can only be made after examination of different portions of the growth. Both benign and malignant areas may be found within a single tumor. The majority of these growths appear to be malignant when first encountered (Hryntschak found only 6 benign cases in a series of 63 collected from the literature). This, coupled with the fact that primarily benign lesions frequently undergo malignant changes, or, following removal, recur in a malignant form, makes it necessary to consider all papillary tumors of the renal pelvis as potentially malignant.

Papillary tumors of the renal pelvis may exist as single lesions, but usually are multiple. They may be extremely numerous, covering the entire mucosa of the pelvis and calyces, blocking off the latter. The papillary tumor is not nearly as malignant as the non-papillary type, but shows a marked tendency to spread downward to the ureter and bladder by direct extension and implantation. Kimball and Ferris (1934) collected reports of 74 cases from the literature, in 50 of which metastases appeared in the ureter and bladder; in 24 cases the ureteral orifice was involved, in 18 cases both the ureteral orifice and the bladder. Occasionally, there is seen one large tumor, with small growths scattered over the ureter and, sometimes, the bladder. As a rule, the associated tumors are similar in their histological structure to the pelvic neoplasm. The primary tumors do not confine themselves to the pelvis and calyces, but may invade the parenchyma of the kidney. In advanced cases, multiple areas are usually to be found in the renal cortex. Metastases occur to the regional lymph nodes, as well as to the lungs, liver, adrenals, and bones.

Various grades of hydronephrosis and back-pressure changes often result from partial occlusion of the ureteropelvic junction either by the original tumor or by ureteral transplants. Whether by hydronephrosis or by the tumor mass itself, the pelvis is distended in the majority of cases.

Non-Papillary Tumors. Non-papillary carcinomas of the renal pelvis are much less common than the papillary tumors, but occur with sufficient frequency to be of considerable clinical importance. Squamous-cell carcinomas make up the major part of this smaller group.

The alveolar carcinoma is large, infiltrating, highly malignant, and metastasizes rapidly to any part of the body. It is probably a far-advanced papillomatous growth which has lost its papillary character and has assumed an alveolar or scirrhous type of growth (MacKenzie and Ratner).

The squamous-cell carcinoma of the renal pelvis is a highly malignant tumor which has an insidious onset and runs a rapid and fatal course. Gilbert and MacMillan, in an exhaustive study of the literature in 1934, collected 57 proven cases, including 2 of their own; to these Kutzmann (1938) added 15 cases not included in Gilbert and MacMillan's survey, as well as 8 later cases and 1 personal case. Lazarus (1938) reported 1 case, making a total of 82 cases up to 1938. Chronic infection, leukoplakia, and calculus are frequently associated with squamous-cell carcinoma of the renal pelvis and are believed to play an important role in its causation.

The squamous pelvic tumor is a grayish, extensively indurated, infiltrating growth which extends over a limited portion of the mucosa. These carcinomas are usually quite large, and are of the flat and ulcerative type, but occasionally they tend toward a papillary formation. Microscopically, the squamous qualities are usually seen to be pronounced. There is often cornification and pearl-formation. Occasionally, a form of less well-differentiated squamous-cell carcinoma, with lessened or no cornification, is encountered; this is a less characteristic type and is often confused with some of the other carcinomas of the papillary type in the renal pelvis. The squamous-cell tumors are highly malignant and present a very poor prognosis since they early invade the surrounding structures. They have a tendency to infiltrate the pelvic wall, with secondary involvement of the kidney. Direct extension to the vena cava and to the regional lymph nodes occurs quite often, and metastases to the lungs, adrenal, peritoneum, bones, and vertebrae are common.

Signs and Symptoms. There is no pathognomonic clinical syndrome. Hematuria, pain, a palpable tumor in the kidney region, and the passage of tissue comprise the chief signs and symptoms.

Hematuria, which usually is intermittent and, in the papillary tumors, profuse, is the most frequent symptom (70 to 80 per cent of the cases). The blood gradually increases in amount and later gives rise to clots, the passing of which may be painful. Obstruction of the ureter by a clot may result in hematonephrosis. The solid epidermoid tumors, being more avascular, do not usually cause as profuse bleeding as the papillary growths.

Tumors located at the pelvic outlet early produce obstruction with retention. In cases with hydronephrosis or hematonephrosis due to obstruction, the enlarged organ can be readily felt; otherwise the palpatory findings are likely to be negative.

Pain is not a constant symptom, but is present in many cases. When due to an obstructive hydronephrosis, it is dull in type and localized to the kidney area; when caused by obstruction due to blood clot, tumor tissue, or associated calculus, it takes the form of a typical renal colic. Pain is a more prominent symptom in the non-papillary tumors, which is probably due to the more frequent association of concomitant disease, such as calculus and severe infection.

The passage of tissue is not infrequent and is highly suggestive. Urinary symptoms—frequency, urgency, dysuria—occur when there is concomitant infection or when the bladder is irritated by blood clots or pieces of tissue.

Loss of weight and strength, anemia, and cachexia occur late and with metastases.

Diagnosis. The preoperative diagnosis of renal pelvic tumor is relatively difficult. In the past, a diagnosis of parenchymal tumor has been made in most cases and the primary pelvic involvement revealed upon surgical intervention. There is no known method of clinically differentiating between the papillary and squamous-cell tumors, and a preoperative diagnosis of the latter is not known to have been made. Of 55 cases of squamous-cell carcinoma collected by Gilbert and Mac-Millan in 1935, the preoperative diagnoses were as follows: tumor, 20; renal calculus, 20; pyonephrosis, 3; tuberculosis, 1; no diagnosis, 11.

The diagnosis is based on the history, examination of urine, and cystoscopy and pyelography.

A history of intermittent hydronephrosis, with hematuria and dull or colicky pains, is extremely suggestive of a pelvic or ureteral neoplasm, but may also occur with other pathological conditions of the upper urinary tract.

Examination of the urine is frequently more significant in tumors of the renal pelvis than in those of the parenchyma. Sometimes particles of tumor tissue may be discovered in the urine obtained by ureteral catheterization—an important diagnostic point. Severe bleeding after the introduction of a catheter into the pelvis or upper ureter should arouse suspicion of a renal pelvic tumor.

Cystoscopic examination is important in order to determine the site of the bleeding and the function of the opposite kidney. Inspection of the bladder may reveal tumor transplants about a ureteral orifice or in the adjacent vesical wall, which may confirm the suspicion of similar tumors in the pelvis or ureter.

The diagnosis of renal pelvic tumor is made chiefly by urographic study. Intravenous urography may be of assistance in certain cases, but delineation by this means is seldom as cleancut as by retrograde pyelography. Sometimes, however, ureteral catheterization may be impossible and intravenous urography must then be relied on.

Depending on the size and location of the tumor, the pyelogram may disclose filling defects and disturbances of the normal contour of the renal pelvis. A primary pelvic papillary epithelioma may be so small as not to give a filling defect in the pyelogram. Even when defects are present, they are often difficult to interpret aright. If the tumor lies in the pelvis, there may be distention of the pelvis, with, often, an apparent obliteration of one or more of the calyces due to blockage of the primary calyx or calyces by the tumor. The contour of the pelvis may be hazy and irregular. Hydronephrosis may be present, and when associated with complete blockage at the ureteropelvic junction, may be very large. The kidneys may be of normal size and contour, or enlarged and irregular.

The filling defects noted in the pyelogram may be the result of tumor or of (1) non-opaque calculi, which sometimes produce filling defects that simulate those due to intrapelvic or intracalyceal tumors (these can usually be excluded by passing wax bougies and obtaining definite scratches); (2) inflammatory granulomas and pyelitis cystica; (3) incomplete filling of the pelvis due to insufficient dye; (4) blood clots in the pelvis or ureter, or a combination of tumor and blood clot. The definite exclusion of blood-clot filling defects may be difficult or impossible. Lavage of the pelvis and ureter, with the subsequent repetition of pyelo-ureterography, and comparison of the pyelograms taken before and after pelvic lavage, will usually help to clarify the diagnosis.

Nephrotomy and careful inspection of the kidney is the only satisfactory means of diagnosis when the history and urological study point strongly to tumor.

Differential Diagnosis. The chief pathological conditions to be differentiated are tuberculosis of the kidney, renal calculus, pyelonephritis, and tumors of the renal parenchyma.

Prognosis. The prognosis of non-papillary tumors is very poor. The primary mortality of squamous-cell tumors is high, and even those who survive the operation usually die within 6 to 9 months. There is no 5-year cure on record. These tumors are highly malignant, and early invade the renal parenchyma and retroperitoneal tissues, and metastasize extensively to distant organs and tissues. It is apparent that if

the patient is to live, very early treatment must be instituted. Unfortunately, the majority of these patients are not seen until the growths have extended beyond the hope of cure.

Alveolar carcinoma also tends to run a rapidly fatal course, metastasizes early and widely, and carries a very poor prognosis.

In papillary tumors, the prognosis is somewhat more favorable. Papillary carcinoma is the less malignant of the cancerous lesions of the renal pelvis, runs a slower clinical course, and offers the better prognosis. It metastasizes by implantation into the ureter and bladder, or extends directly into the ureter, but distant metastases occur late and are not widespread. Generally speaking, if not too far advanced, this tumor offers a relatively good prognosis when treated by nephro-ureterectomy with removal of the adjacent portion of the bladder wall.

The papilloma is a benign growth, but clinically it is potentially malignant and has a tendency to involve the ureter and bladder by implantation. Recurrences following removal are common and may occur many years after treatment, and such recurrences are usually carcinomatous. The prognosis should therefore be guarded.

Treatment. Because of the frequency of secondary implantation along the urinary tract, the operation of choice in most cases of papillary tumors of the renal pelvis is nephro-ureterectomy, with resection, or destruction by diathermic means, of that part of the bladder wall which includes the intramural portion of the ureter. Less radical procedures have proved, in the past, insufficient for a cure. Not only in papillary carcinoma, but in simple papilloma as well, there is a high incidence of recurrence in the ureteral stump or bladder following conservative surgery, making later intervention necessary. In all cases, whether the ureter is involved or not, we advise that the duct be removed, together with the portion of the bladder wall containing the ureteral orifice. This we do because in two of our own cases the ureter was not involved at the time nephrectomy was done; nevertheless, both of these patients died from carcinoma of the bladder—one 2 years and the other 5 years after nephrectomy. Occasionally, because of the patient's poor condition, it may be advisable to perform nephro-ureterectomy in two stages, the nephrectomy first and later the ureterectomy.

Early nephrectomy is the only treatment known for the highly malignant, infiltrative, non-papillary tumors, and this has been of little avail since no 5-year cures are known. Since these tumors possess little tendency to involve the ureter and bladder, the usual nephrectomy, with

removal of the upper portion of the ureter, suffices. The results of surgery have been very unfavorable in these cases since, as a rule, the growths have already transgressed the boundaries of the pelvis when they came under observation, and extensive secondary infection are usually present.

Judging from the absence of reports in the literature, the use of deep x-ray therapy is of little value in the treatment of tumors of the renal pelvis, though a few make use of it postoperatively and in advanced, inoperable cases.

(2) *Tumors of the Renal Parenchyma in Children*

Malignant tumors of the renal parenchyma which occur in the first decade of life differ markedly from malignant renal tumors developing in adult life. The former are of embryonal or teratoid origin; the latter are largely of epithelial origin. Adenocarcinoma (hypernephroma) is exceedingly rare in infancy and childhood. The common renal tumor of children is a mixed growth—the so-called adenomyosarcoma of Wilms.

Histologically benign tumors—rhabdomyomas, fibromas, leiomyomas, adenomas, and tumors of mixed adenomatous structure—are of relatively frequent occurrence in children, and usually are multiple. They will be considered in connection with benign renal tumors in adults.

EMBRYONAL ADENOMYOSARCOMA (WILMS' TUMOR)

The commonest renal neoplasm found in children is a mixed tumor of embryonal origin, which has been variously designated, but is most frequently called embryonal adenomyosarcoma, or Wilms' tumor. It is extremely malignant and results in a very high mortality. Only an occasional cure has been reported.

Incidence. With the possible exception of the eye, the kidney is the most common site of malignant tumor in infants and children, the great majority of renal neoplasms being of the Wilms' type. Embryonal adenomyosarcoma is, however, of relatively infrequent occurrence, though the many articles on this subject which have appeared in recent years give one the impression that this is a very common tumor. E. T. Bell (1938) found only 5 examples in 30,000 necropsies "in which children were proportionately represented."

This type of tumor has been observed in the newborn infant and even in an 8-months' fetus (Cutler and Buschke). Three quarters of the cases occur in the first 5 years of life, when other renal neoplasms are very rare. In the later decades, when other kidney tumors are fairly common, one rarely encounters a Wilms' embryoma.

Sex is apparently not an important factor; in some series there is a slight predominance of males, in others of females.

Occurrence is approximately equal on the two sides. In a small percentage of the cases there is bilateral involvement; when this occurs, it may be difficult to ascertain whether both tumors are primary or whether one is a metastatic growth.

A familial tendency is noted by some observers. Deutike (1931) reports a case in a 2-year-old child whose brother had died with a similar tumor at the same age. Maslow (1940) published a report of 3 cases and a possible fourth in the same family; these were collected at the Urological Clinic in the University of Budapest, Hungary.

Pathogenesis of Wilms' Tumor. The origin of mixed renal tumors has been the subject of much controversy, and the facts of pathogenesis are still largely a matter of surmise. Most present-day observers agree that the tumors are embryonal in that they arise in the region of the developing kidney. The various theories of origin have been summarized as follows (Fraser):

1. The tumors owe their origin to inclusions of wolffian tissue which have become displaced, and which persist among the cells of the developing kidney or metanephros.

2. The tumors arise from aberrant cells of the myotome and sclerotome, the apparent mixed character being explained by the varying constituents which enter into the ultimate formation.

3. The tumors are not due to inclusions from extrarenal sources, but they are true kidney, the embryonic tissue persisting and becoming metamorphosed into cellular structures of various types.

Eberth, in 1872, gave the first accurate histological description of a mixed tumor of the kidney. Prior to that date, all malignant tumors of the kidney, both in children and in adults, were considered as being of a carcinomatous nature. Eberth called attention to the heterogeneous character of the tumor, and attempted to explain the presence of the muscular elements by attributing their origin to inclusions of the wolffian body, the connective tissue of which contains an abundance of embryonal muscle cells. The theory of origin from the wolffian body is associated chiefly with the name of Birch-Hirschfeld, who, in 1894, reviewed the cases of mixed renal tumor in the literature and was the first to designate the growth as embryonic *adenosarcoma*. Busse subsequently challenged the theory of Eberth and Birch-Hirschfeld on the ground that remnants of the wolffian body did not appear ever to have been found in the human kidney.

Wilms, in his classical monograph on mixed renal tumors, published in 1899, postulated that these growths originate very early in embryonic life from fragments of primitive undifferentiated mesodermal tissue of a type which, in the course of normal development, gives rise to the cells of the myotome (source of striated muscle), the sclerotome (primitive vertebral tissue), and the nephrotome (wolffian body anlage). Some of these undifferentiated cells may concentrate at the site of the developing kidney and, through a process of metaplasia, may later give rise to tumor masses in which may be found striated muscle, smooth muscle, and cartilage. Fifty-one cases of mixed renal tumors were analyzed by Wilms, who established this lesion as an entity.

A theory directly opposed to Wilms' view is that advanced in 1899 by Busse, namely, that the mixed renal tumor arises at a much later date, from the metanephros, and that the various types of tissue develop by a process of metaplasia. Muus, in the same year, called attention to the similarity of this type of tumor and the histological structure of the embryonic kidney.

The hypothesis that these tumors arise from the embryonic tissue of the true kidney later received support from Nicholson (1931), who regarded the presence of glomeruli as evidence of metanephric origin. This author is of the opinion that the mixed renal tumor represents natural and physiological forms of growth "which can be referred to the action of elementary biologic principles, instead of the pathological and monstrous theories devised to explain them." He examined an embryonal renal tumor from a full-term fetus, and states that the tumor resembles, and represents, a malformed embryonic kidney. Stern and Newns (1937) object to this view on two grounds: (1) that it cannot explain the presence of the muscle fibers which have been observed in a fairly high proportion of these tumors, and (2) that the tumors are seldom in or incorporated with the kidney. They argue that "if the tumors are to be regarded as part of the developing kidney, it would be expected that they should be incorporated in the kidney substance and situated in the interior of that organ."

Ewing also favors the theory that these tumors are derived from the renal blastema.

Geschickter and Widenhorn (1934) relate mixed renal tumors to embryonic nephrogenic tissue. Approximately two-thirds of all Wilms' tumors, they claim, are neither teratomatous nor mixed, but "represent a neoplastic exaggeration of the normal developmental processes occurring in

the growth zones of the renal cortex in the late fetal life or in the first few months after birth." They state that the presence of muscle, cartilage, or bone in the remaining one-third of these tumors is readily understood when one considers "that the more undifferentiated mesenchymal spindle cells found in the normal nephrogenic tissue in the process of development may retain the multiple potentiality for the elaboration of all the normal mesenchymal derivatives."

From a careful review of the various theories of pathogenesis, we get the impression that modern observers are about equally divided between (1) the theory that these tumors originate very early in embryonic life, from a multipotential cell, and (2) the theory that they originate at a much later stage, from the embryonic tissue of the true kidney.

Pathology. The Wilms' tumor is a large, solid, grayish-white, encapsulated tumor of variegated histology. It is usually separated from the kidney by a layer of tough connective tissue. The capsule of the tumor blends with that of the kidney and with this membrane. Occasionally, the tumor will be found to fuse with the kidney, but usually it is well delimited from the renal tissue until late in the course of the disease, when invasion and perforation of the capsule occur. While still confined by its intact capsule, the tumor tends to maintain a spherical shape; but when the capsule is broken through, the unrestrained tumor rapidly sends out irregular projections into the surrounding tissues. Hemorrhagic or softened areas, and a more or less cystic structure are not uncommon findings.

These tumors appear to favor the lower pole of the kidney, but they have often arisen from the upper pole and from the middle (convex) portion of the kidney. Following a period of relatively slow activity, they grow rapidly and to a large size. Growth is by expansion rather than by infiltration. The tumor rapidly destroys the kidney, mainly by compression—the expanding growth usually causing pressure atrophy of the kidney remnant. The pelvis of the kidney may be normal or dilated, but usually is compressed.

Histologically, these tumors are composed of a variety of tissues, and the microscopic picture will naturally vary with the types of tissue present and predominating. The distinctive feature which they have in common is the association of epithelial with connective tissue. In some instances, a great variety of tissues may be found in a single growth. In others, one type of cell may predominate. Probably, many cases reported as sarcomas in the literature actually are mixed tumors which

have undergone development in one direction. Frequently, the adenosarcomatous elements predominate, while occasionally the picture will resemble that of a carcinoma. Rudimentary glomeruli are seen fairly often. Other elements found in these tumors are non-striated and striated muscle fibers, cartilage, myxomatous tissue, and, occasionally, bone and fat. At present, the histological classification of these heterogeneous renal tumors occurring in infancy and childhood is of interest only to the pathologist. Clinically, despite their varied histological features, they are considered as one group.

Metastases and Extensions. The tumors metastasize relatively late, despite their high degree of malignancy and rapid growth. Metastases are chiefly by way of the blood stream to the lungs and liver. After the tumor has broken through its capsule, there is involvement of the retroperitoneal nodes and extension to the neighboring structures by direct infiltration. Fixation to the liver, pancreas, colon, duodenum, stomach, or aorta occurs in a high percentage of the cases. Extension into the renal vein or its branches, and invasion of the renal pelvis, are often encountered. The tendency of these tumors to recurrence following removal is pronounced.

Signs and Symptoms. The symptom that leads to the discovery of the tumor in the great majority of cases is the presence of a swelling on one side of the abdomen, in the upper quadrant. This is usually painless, and as a rule is first noted by the mother or nursemaid when bathing the child. The swelling is always progressive. The size of the tumor varies in each case. Occasionally it may be so large as almost to fill the abdomen.

The presence of a tumor mass is the only constant symptom in these cases. However, a number of other symptoms are often associated with the tumor: pain, weakness, pallor, fever, gastrointestinal disturbances, and hematuria. Fever is a common symptom. Pain, as a rule, does not occur until later in the course of the disease, when adhesions have formed or the tumor has attained sufficient size to press upon other organs. The pain may also be due to tension on the peritoneum and the nerve plexus by the weight of the mass. Growth of the tumor displaces the intestines, producing gastrointestinal disturbances, such as nausea, vomiting, colicky pain, and constipation; while upward displacement of the diaphragm causes interference with breathing. Pressure on the abdominal veins may produce edema of the lower extremities. Apathy, loss of weight, and symptoms of marked anemia are frequently noted.

These usually occur with progress of the disease; but sometimes listlessness, pallor, and anorexia are the first symptoms observed, and anemia and emaciation develop early.

In general, urinary symptoms are of secondary importance in these cases. Often they are absent. Frequency, burning on urination, albuminuria, and hematuria are the symptoms most often noted. In rare instances, pressure on the opposite ureter by the tumor may cause anuria; or anuria may occur by reflex action from the diseased kidney.

Hematuria is infrequent (10 to 25 per cent of the cases, Dean and Pack). It is always intermittent, and is not an early sign. Though hemorrhage within the tumor is common, the delimitation of the tumor from the kidney, and the fact that the walls of the calyces remain intact in most cases, prevents the blood from entering the urine.

Hypertension is often associated with Wilms' tumor (14 of 18 cases, W. E. Daniel, 1939), and has been attributed to the renal ischemia. Bradley and Pincoffs reported 5 cases of Wilms' tumor with hypertension; in all 5 cases the hypertension was cured by removal of the tumor, but in 2 it recurred with recurrence of the metastases. These authors therefore feel that the tumor tissue in these cases must have a property possessed by renal tissue when it has been altered by certain types of damage—namely, the property of causing, through as yet unknown mechanisms, an abnormal elevation of the arterial pressure.

Diagnosis. The diagnosis of Wilms' tumor in a child is not usually very difficult. It is based on the clinical history, physical examination, and pyelographic evidence.

The main symptoms are those of enlargement of the abdomen and symptoms due to pressure on the adjacent organs.

On abdominal palpation, the tumor usually feels solid, smooth, and rounded, though occasionally it feels nodular. As a rule, it is not tender. By bimanual examination, the tumor's location in the kidney region can be determined. The veins over the abdomen may be dilated because of compression of the vena cava by the tumor. Ascites and terminal edema may be present.

The plain x-ray is rarely diagnostic.

Cystoscopy and pyelography, on the other hand, may give valuable diagnostic and differential diagnostic data, as well as essential information regarding the presence and functional ability of the opposite kidney. No infant of either sex is too young for a complete urological examination. Intravenous urograms are usually less satisfactory. The most

frequent pyelographic findings are (1) compression and elongation of the calyces and pelvis; (2) lateral displacement of the renal pelvis by the tumor mass, or downward displacement if the tumor arises from the upper pole; (3) failure of the pelvis to visualize. Kretschmer states that the last may be due to the fact that there is only a small amount of functioning parenchyma left, or, in the case of a large tumor, to obscuration of the pelvic outline by the tumor shadow. It must be remembered that an absolutely normal-appearing pyelogram may exist in the presence of a very large embryoma.

Aspiration biopsy, or incision of the tumor to obtain histological material, is unsafe and unwise, since once the capsule is disrupted, the chief defense against rapid extension of the tumor and implantation is broken down.

Differential Diagnosis. Though the Wilms' embryoma is by far the most common abdominal tumor in children, certain other tumors must be considered in the differential diagnosis. Those most likely to give difficulty are: the relatively common neuroblastoma which arises from the medulla of the adrenal gland and which also is of rapid growth (pre-operative differential diagnosis may be impossible); adenocarcinoma (very rare in childhood); and the retroperitoneal embryoma of renal anlage origin. Wilms' tumor must also be differentiated from polycystic kidney, tumors of the liver, omental and pancreatic cysts, ovarian tumors, and splenic enlargements. The last are distinguished by the blood picture.

Prognosis and Treatment. There is some difference of opinion as to the most desirable plan of treatment of these tumors. Nephrectomy and deep x-ray therapy, alone or in combination, are the methods of treatment now being utilized. Neither form of treatment has given satisfactory results. The prognosis in these tumors is always very grave. Without treatment, the child invariably dies, usually within a relatively short period of time. With treatment, by any of the accepted methods, the results are almost equally cheerless. The mortality, early and late, is extremely high, due to the large size which the tumor generally has reached when it comes under observation, and to the high malignancy of the growth and the strong tendency to recurrence. The reports of cures, the duration of which can be stated in years, are very few.

The malignant renal growths of young children can often be removed with surgical success, but the likelihood of recurrence is so great that the outlook in all cases is exceedingly gloomy. In some cases, metastasis

begins early, often before the presence of the primary growth is suspected. The surgeon must constantly keep in mind the fact that the size of the tumor mass is no criterion of its malignancy, and, unless definite metastases are made out, operation is advisable. Even if metastases exist, and there is great distress due to pressure by the tumor, a nephrectomy will bring sufficient relief to warrant its performance. The age of the child should not influence the decision to operate, since it has repeatedly been proved that nephrectomy can be safely carried out in a very young infant and, without operation, the outcome is inevitably fatal.

The majority of authors at present favor a combination of preoperative deep x-ray therapy and nephrectomy. Most Wilms' tumors are radio-sensitive, though radioresistant forms occur—the degree of response depending upon the proportion of sarcomatous elements (the radio-sensitive portions) to the more radioresistant epithelial constituents. Some authors have attempted to rely upon deep x-ray therapy without nephrectomy, but, with a handful of isolated exceptions, it has not been possible to effect a cure of these tumors by irradiation alone, since the growths recur as rapidly as they regress and recurrences are radioresistant to a greater or less degree.

Preoperative irradiation, by shrinking the tumor, has facilitated operation and reduced the primary mortality in numerous cases, and has frequently rendered inoperable tumors operable. However, it does not appear to have improved the end-results. That irradiation prevents dissemination of the tumor cells is doubtful. Indeed, there are those who believe that it may even facilitate the spread of the growth, since the tumor cells are not completely destroyed and it is probable that the active tumor cells may be picked up and disseminated more rapidly by the blood stream after irradiation than before it.

Though preoperative irradiation, nephrectomy, and postoperative roentgenotherapy have become the therapeutic plan of choice in many clinics, there are some who still feel that preoperative irradiation facilitates the operation and lessens the operative mortality only at the expense of an increased late mortality. A review of the results reported by various authors indicates that, thus far, more apparent cures have been obtained by immediate nephrectomy than by nephrectomy preceded by a course of deep x-ray therapy. However, great strides have been made in roentgenotherapy in very recent years, and, since preoperative irradiation is now being employed in many clinics, it may soon be possible to more accurately evaluate its efficacy in the treatment of these tu-

mors. The small number of apparent cures to date, either by surgery alone or by surgery combined with irradiation, makes it impossible at present to draw definite conclusions as to the superiority of one plan over another.

The most encouraging report we have been able to find to date is that of Dr. William E. Ladd (1938), who reported the results of treatment in 44 cases of Wilms' tumor from the Children's Hospital (Boston). Of these, 31 died, all but one within a year of operation. Of the 14 patients still living at the time of the report, 11 were regarded by the author as probable cures, the length of time since nephrectomy ranging from $1\frac{1}{2}$ to $19\frac{1}{2}$ years ($1\frac{1}{2}$ to 5 years, 4 cases; $5\frac{1}{2}$ to 10 years, 5 cases; 13 years, 1 case; $19\frac{1}{2}$ years, 1 case). All of these 45 patients were treated by nephrectomy. Irradiation was employed in only a very few. While this author, at the time of his report, favored immediate nephrectomy, he recognized that the great strides in roentgenotherapy might possibly soon require a change in viewpoint.

For removal of a tumor of the Wilms' type in a child, the transperitoneal approach is usually preferable to the posterolumbar incision. A rectus or a paramedian incision is the one usually employed. Many of these patients are markedly anemic, and the operation should be preceded by blood transfusion when indicated.

Postoperative irradiation has been employed less extensively than has preoperative roentgenotherapy, but has been found of some value in alleviating symptoms due to recurrence or metastasis, rendering the patient temporarily more comfortable. It is also employed in the belief that it may destroy tumor cells left behind (Radium and Roentgen-Ray Therapy of the Genito-Urinary Tract: Irradiation of Wilms' Tumors, p. 1759).

(3) Tumors of the Renal Parenchyma in Adults

The vast majority of renal neoplasms develop in the parenchyma. Parenchymal tumors are relatively uncommon, however. Prior to the last twenty years, renal tumors in adults were seldom diagnosed except at operation or autopsy. Advances in urographic diagnosis have steadily increased the number of cases recognized clinically, and, consequently, the incidence of renal tumor appears to be greater now than in the past. Though this increase is doubtless more apparent than real, the lesion presents a baffling problem to all practitioners of medicine, and one which demands more intensive study than has heretofore been accorded it.

The only hope of cure lies in the institution of treatment in the early stages, and diagnosis at this stage is extremely difficult.

Age and Sex Incidence. With the exception of the Wilms' tumor, which is almost always encountered in the first decade of life, tumors of the renal parenchyma usually occur after the fortieth year. Carcinomas, the common tumors of the parenchyma in adults, are most frequent in the sixth decade. Sarcoma may occur at any age, but is most common in the fifth and sixth decades.

Renal tumors in adults occur much oftener in males than in females.

Pathogenesis. Since Grawitz, in 1883, published his important studies on renal tumors, many theories of pathogenesis have been advanced, and many names proposed, for the various types of kidney tumors. This is particularly true of the common renal tumor—the large, circumscribed, yellowish, soft growth usually referred to as "hypernephroma," a name given it by Birch-Hirschfeld in 1892. The confusion has been increased by the complexity of the pathological changes and the fact that a single tumor may contain more than one type of cell. Up to the present, theories of pathogenesis remain unproved, and the origin of these tumors is still to be determined.

Grawitz showed that many renal tumors have a histological structure resembling that of the adrenal cortex, and believed that they arose from aberrant adrenal rests. Grawitz's views, though widely accepted, were opposed by Sabourin (1884), Sudek (1893), Albarran and Imbert (1903), Stoerck (1908), and others, who believed that these tumors are various forms of true renal carcinoma, originating from adult renal epithelium.

Although the subject is still unsettled, and no exact classification of renal tumors exists, the present tendency is to confine the terms "Grawitz tumor" and "hypernephroma" to a restricted group of tumors whose structure is similar to that of the adrenal cortex, and to regard as true renal carcinoma most of the growths arising in the renal parenchyma of adults and heretofore referred to as "hypernephromas."

The pathogenesis of Wilms' tumor has already been discussed (Wilms' Tumor: Pathogenesis, p. 1554).

Pathology. Despite the many attempts that have been made in recent years to classify renal tumors, there is as yet no unanimity of opinion regarding their pathological grouping and nomenclature. The confusion is chiefly in the differentiation—if there be any—between the hypernephromas and the clear-cell carcinomas. Clinically, the pathological differentiation of renal tumors in adults is important chiefly from the

standpoint of prognosis and reaction to irradiation. Of greatest importance is the making of a diagnosis which will be sufficiently complete to lead to exploration of the kidney, since the one hope of cure in all cases of renal cancer rests in an early nephrectomy.

The great majority of parenchymal tumors of the kidney arise from the renal epithelium. Tumors of connective-tissue origin and embryonal tumors are relatively rare in adults. Although many present-day authors are inclined to discard the idea of adrenal tumors of the renal parenchyma altogether, a few—notably Ewing—are of the opinion that there is a relatively small group of renal tumors which are undoubtedly adrenal growths, with a structure exactly duplicating that of the adrenal cortex; these should be classified as hypernephromas, and are to be distinguished from the more common clear-cell adenocarcinoma.

Renal tumors may be benign or malignant. Benign growths are supposedly very rare, but the fact that such tumors—usually of small size—are quite often observed at autopsy in subjects who gave no evidence of their presence during life would seem to indicate that they may be more common than has been believed.

It is not our purpose here to enter into the controversial subject of classification and nomenclature. The following classification, we believe, includes the majority of tumors of the renal parenchyma:

- | | | |
|--|---|----------------------------------|
| 1. Carcinoma | } | Epithelial tumors |
| (1) Papillary adenocarcinoma | | |
| a. Clear-cell (confused with hypernephroma) | | |
| b. Granular-cell | | |
| c. A transition form, containing both types of cells | | |
| (2) Alveolar carcinoma | | |
| (3) Malignant papillary cystadenoma | | |
| 2. Adenoma | | |
| 3. Sarcoma, spindle-cell | } | Connective-tissue tumors |
| 4. Fibroma: fibrosarcoma | | |
| 5. Lipoma: liposarcoma | | |
| 6. Leiomyoma: leiomyosarcoma | | |
| 7. Myxoma: myxosarcoma | | |
| 8. Hemangioma | | |
| 9. Adenomyosarcoma (Wilms' tumor) | } | Embryonal tumor |
| 10. Hypernephroma | } | Tumor arising from adrenal rests |

Carcinoma. Carcinoma is the commonest form of parenchymal tumor in adults. Three varieties require consideration: (1) adenocarcinoma, (2) alveolar carcinoma, and (3) malignant papillary cystadenoma. A single tumor may contain features of each variety. Regardless of their histological peculiarities, the behavior of this group is sufficiently uniform to justify their consideration as a clinical entity.

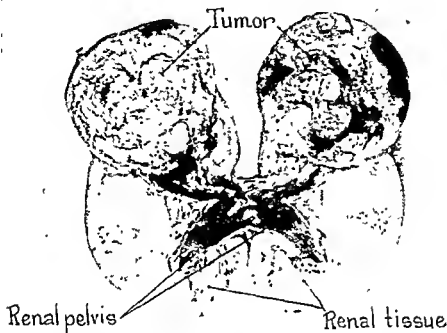


FIG. 327. Large adenocarcinoma projecting from the upper pole of a left kidney. Operative specimen. The tumor mass is embedded in the renal substance and has grown into the upper part of the pelvis.

PAPILLARY ADENOCARCINOMA. Three types of adenocarcinoma have been distinguished.

Clear-cell papillary adenocarcinoma histopathologically often resembles carcinomas arising from the cortex of the adrenal, but is probably derived from the collecting tubules of the kidney and not from aberrant adrenal rests. These tumors were first described by Grawitz, and, until recently, were usually referred to as Grawitz tumors or hypernephromas.

This type of tumor is usually large, single, well circumscribed, and often encapsulated. It may arise from the cortex or the medulla, and is frequently located at either pole, though almost as often it occupies

the middle of the organ. On cross section, it has a characteristically yellowish appearance, and shows necrotic and hemorrhagic areas, with, sometimes, pseudocystic areas which have followed necrosis. Histologically, it is composed of papillary strands of connective tissue covered by large, very clear cuboidal or cylindrical epithelium. The tumor has a strong tendency to invade the renal vein and to produce blood-borne metastases in distant organs.

There is also a type of papillary adenocarcinoma with more granular cells suggestive of convoluted-tubule origin. This type is non-fatty, less vascular, and whiter in color than the clear-cell type. Such carcinomas are more apt to spread by the lymphatics than by vein. They infiltrate the renal parenchyma and do not produce the large, nodular growths more commonly seen.

A third, transition form of adenocarcinoma contains both the clear and granular types of cells.

ALVEOLAR CARCINOMA. Alveolar carcinoma is a very malignant form. Microscopically, it shows solid cords of clear or granular cells. Differentiation between adenocarcinomatous and alveolar forms is frequently difficult, since a single tumor will sometimes show features of both.

MALIGNANT PAPILLARY CYSTADENOMA. The malignant papillary cystadenoma is a rare and confusing form of carcinoma of the renal parenchyma, which is to be distinguished from papillary adenocarcinoma. Ockerblad and Carlson found 15 reported cases up to 1938, and added 1 case of their own, which occurred in a double kidney. The tumor is well encapsulated, comparatively slow growing, and metastasizes fairly late, so that the prognosis is somewhat more favorable than that of the usual renal tumor. Some of these growths plainly show the transitional stages from benign adenomas.

DEGREE OF MALIGNANCY. The gross appearance of a renal carcinoma differs with the degree of malignancy and of vascularity, and the presence or absence of necrosis, hyalinization, fibrous tissue, and fat. Generally speaking, small, well-encapsulated, vascular tumors are of a lower grade of malignancy than the large, degenerating carcinomas which involve almost the entire kidney and those which infiltrate the renal parenchyma and grow toward the pelvis (Hand and Broders).

The size of the tumor is not a certain criterion as to its grade of malignancy. In general, the large tumors are more apt to have formed metastases.

METASTASIS AND EXTENSION: RECURRENCE. Spread of the tumor takes place in the following ways: (1) metastasis through the blood stream, either (a) by invasion of the renal vein, (b) by microscopic emboli which enter smaller vessels, or (c) extension into the vena cava; (2) metastasis through the lymphatics; (3) direct extension through the capsule; (4) direct extension to the renal pelvis, and thence to the ureter and even into the bladder.

Metastasis through the blood stream is by far the most common. The clear-cell papillary adenocarcinoma, in particular, has a strong tendency to invade the renal vein and to produce distant blood-borne metastases in lung, liver, bone, and brain. The true infiltrating carcinoma is more apt to spread by the lymphatics than through the vascular channels. Direct extension to the perirenal tissues occurs very frequently.

Local recurrence following nephrectomy is common, and, thus far, deep x-ray therapy has not been very successful in preventing or controlling such recurrences. Both local recurrence and distant metastasis may occur many years after nephrectomy.

Adenoma. Because adenomas, especially those of large size, are seldom seen, but little attention has been given them when discussing renal neoplasia. Cases have been reported, and the subject discussed, by Kretschmer and Doehring (1929), Gordon-Taylor (1930), and Bailey and Harrison (1937).

Small adenomas, varying in size from 2 mm. to 1 cm. or even larger, are a relatively common postmortem finding in arteriosclerotic kidneys. They usually occur in the form of multiple discrete, whitish nodules located just beneath the renal capsule, or they may be scattered over the renal parenchyma. They often occur bilaterally. Histologically, they are made up of irregular groups of epithelial cells ranged around lumina which are irregular in outline. Papillary projections of epithelial-cell masses into such a lumen are a frequent observation. The epithelium, however, is present only in a single layer, the resemblance to normal renal tubules being so close as to be frequently difficult of differentiation. Seldom is a mitotic figure observable. A definite connective-tissue capsule, uninvaded by epithelial cells, is usually found. These small adenomas are slow-growing, symptomless, and essentially benign, and have no clinical importance.

The large adenomas, however, frequently give rise to hematuria and pain. Furthermore, they are potentially malignant. These tumors

are usually single. Histologically, they are similar to the small growths, but as a rule their structure will have been broken down by extensive necrosis. Grossly, they appear as large, circumscribed, cortical tumors of a yellowish or whitish color. Though classed as benign, they are potentially malignant and should always be viewed with suspicion. No certain distinctions can be made between adenomas and carcinomas.

Large adenomas may occur at any age, even in very young children.

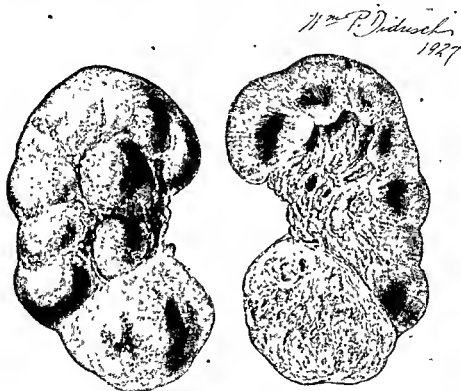


FIG. 328. Osteoma of the kidney. (Specimen from collection of Dr. Marion)

Sarcoma. Sarcoma of the kidney is very infrequent in adults. Over 50 per cent of the reported cases have been encountered in persons between the ages of 40 and 60 years. The histopathological structure of these tumors varies considerably, but they are all highly malignant and almost invariably terminate fatally irrespective of treatment. Spindle-cell sarcoma is the most common type, with fibrosarcoma, liposarcoma, leiomyosarcoma, and other forms of very rare occurrence.

The symptomatology, diagnosis, and treatment are the same as in other large parenchymal tumors.

Fibroma; Fibrosarcoma. Fibromas of the kidney, like adenomas, occur in two forms: (1) as small, whitish nodules, which rarely cause symptoms and are usually discovered at autopsy or operation for other causes; (2) as large, cortical growths which produce symptoms and require surgical treatment. These larger tumors are very rare, and may occur at any age. A number have been reported in young children. In most of the reported cases, nephrectomy was done; but if the tumor is not too large, and its benign character can be unquestionably demonstrated, resection of the growth may suffice.

Fibrosarcoma of the kidney appears to be excessively rare.

Lipoma; Liposarcoma. Small, multiple lipomas beneath the renal capsule or elsewhere in the cortical tissue are sometimes encountered. Although occasional large lipomas have been reported, it is generally believed that true lipomas rarely attain a size greater than 1 cm. in diameter. It is probable that most of the larger lesions are, in reality, replacement lipomatosis, which originates from the pelvic fat (Replacement Lipomatosis, p. 1485).

A few liposarcomas have been reported.

Leiomyoma; Leiomyosarcoma. Benign leiomyomas, of a size to produce symptoms, are seldom encountered. In 1899 Oschner removed a leiomyofibroma which weighed 4,600 Gm. Scattered reports of isolated cases are to be found in the literature beginning with the present century. Several leiomyosarcomas, usually of large size, have been reported in recent years (N. E. Berry, 1929; Crosbie and Pinkerton, 1932; Cooke, 1933). In 1939, Gordon and his colleagues summed up the 28 previously reported cases of various forms of renal leiomyoma and added a personal case.

Leiomyomas, like other benign growths of the renal parenchyma, occur in two forms: (1) small growths found at autopsy in subjects who have died from unrelated causes, having given no symptoms during life; (2) *growths which become large enough to produce pressure and other symptoms, so that they are discovered during life.* Tumors of the first class are often multiple and are to be found just beneath the renal capsule. They probably arise from the smooth muscle of the capsule or from the muscle of blood vessels. *Of the growths large enough to cause symptoms, the literature offers only a few examples.* Macroscopically and microscopically, these tumors are similar to the common leiomyoma of the uterus. Because they grow rapidly, and sometimes reach a very large size, and are potentially malignant, nephrectomy may be advisable.

Hemangioma. Hemangiomas are occasionally encountered, but unless they attain considerable size and cause pressure or other symptoms, are of no clinical importance. Hematuria does not occur unless the tumor erodes the renal pelvis.

Wilms' Tumor. The mixed, or Wilms' tumor, of embryonal origin is usually found in the first decade of life, but in rare instances occurs in adults. The structure is usually that of adenomyosarcoma. This tumor has been described in detail elsewhere (Wilms' Tumor, p. 1553).

Bilateral Primary Malignant Tumor of the Kidney. Bilateral primary renal neoplasm is excessively rare. Forsythe, reporting a case of bilateral primary hypernephroma from the Brady Foundation, of the New York Hospital, in 1942, carefully reviewed the literature but was able to find reports of only 6 other cases. Several of these, he felt, may have represented metastatic lesions, and one a polycystic kidney.

The patient seen at the Brady Foundation, a 62-year-old male, had complete urinary retention following hematuria of 3 days' duration. He had had painless hematuria of 1 day's duration 3 years previously. Examination revealed a greatly enlarged, adenomatous prostate, and moderate abdominal distension, but no palpable abdominal masses. As it was thought that the bleeding was either prostatic or vesical in origin, catheter drainage with intermittent irrigation was instituted, with little change in the hematuria. Excretory urography showed poor function of the left kidney and no function on the right side. Cystoscopy was unsuccessful, due to bloody urine. Because of continued bleeding, a suprapubic cystostomy was done under local anesthesia. No bladder tumor was found and the source of the bleeding was not discovered. The patient's condition improved after cystostomy. Excretory urograms, a week later, showed no function on the right side and definite enlargement of the right renal shadow. At this time, the right kidney was palpable and much enlarged. Cystoscopy was repeated and gross blood was seen exuding from the right ureteral orifice. A right retrograde pyelogram showed an apparent renal neoplasm with probable extension to the pelvis and upper ureter. A right nephrectomy was done, after supportive treatment, including transfusions; and a kidney with extensive tumor involvement was removed. There was extension, which was inoperable, into the pedicle. The patient expired of cardiac failure 48 hours after operation.

Autopsy revealed tumor in the remaining portion of the pedicle and a tumor thrombus in the vena cava. In the midportion of the left kidney

was a tumor about 4 x 6 cm.; grossly this appeared to be a separate primary growth. Careful search, including x-raying of the long bones, failed to disclose any metastatic lesion. Examination of the heart showed an organized thrombus in the left coronary vessel. Microscopically, the tumor in each kidney showed a similar picture, being composed of large, clear vacuolated cells with small nuclei. The cells grew in cords and masses, and were well differentiated. It was felt by the pathologist that each tumor represented a primary lesion, although it was realized that a hypernephroma may give rise to a solitary metastasis.

Signs and Symptoms of Parenchymal Tumors. Hematuria, pain, and tumor have been well impressed upon the medical profession as the classical triad of cardinal symptoms pointing to renal tumor. These are common symptoms of other renal lesions, and are never pathognomonic. Although all three are frequently present when the patient is first seen by the urologist, diagnosis at this stage cannot be considered an early diagnosis. Pain and tumor are usually late manifestations; by the time they occur, the tumor is generally far advanced and metastases are often present, so that the patient is beyond surgical relief.

Hematuria is the most constant and outstanding symptom of tumor of the kidney. It is particularly important because, in the renal cancers of adults, it usually is the earliest symptom, and appears at a stage when the tumor is not yet palpable. In Wilms' tumor in children, as well as in the rare, large, benign growths, a palpable tumor is usually the earliest symptom, with hematuria a relatively late manifestation.

The bleeding is always intermittent and is seldom profuse. Intense hemorrhage sometimes occurs, however. Generally the bleeding does not last longer than several days. A single severe hemorrhage may be followed by months or even years of freedom from hematuria. As a rule, bleeding from a renal tumor does not produce clots, the blood being diffused in the urine. Occasionally, however, the bleeding is sufficiently profuse to cause a blood cast of the ureter; when this happens, the outflow of urine is impeded, resulting in marked pain due to back pressure.

Pain is the second most important symptom. It is present in a large percentage of the cases in the later stages of the disease, and is the initial clinical symptom in about 20 per cent (Israel and Israel). When present in association with hematuria, pain is of value in determining the source of the bleeding. Pain may be caused by stretching of the renal capsule by the enlarging tumor, or it may result from pressure by the mass on the nerves or on neighboring viscera. Pressure from a large tumor may be exerted (1) upward, with embarrassment of respiration, (2) downward,

causing symptoms referable to the pelvic organs, or (3) anteriorly, with displacement of the spleen and colon. Intermittent colicky pain may occur as the result of tension due to hemorrhage within the tumor, or when there is obstruction of the ureter with blood clots.

Other late symptoms are loss of weight (common), weakness, gastrointestinal disturbances, fever, symptoms of anemia, and cachexia. The detection of a metastatic growth may be the first clue to the presence of a neoplastic process.

Diagnosis. Success in the treatment of renal tumors is in direct proportion to their early recognition. Early diagnosis of renal neoplasm is, however, particularly difficult, since the disease is insidious in its onset and there is no one symptom, or group of symptoms, which points indisputably to renal malignancy. Painless hematuria being the earliest manifestation in most cases, discovery of these tumors at a stage when cure is still possible depends largely upon impressing on the medical profession itself, as well as the laity, that the presence of blood in the urine is a sign of the gravest import, which merits complete investigation of the urinary tract. The emphasis placed by urologists on the significance of painless hematuria is gradually bringing more renal neoplasms under observation at an earlier stage of development than in the past.

The diagnosis is made upon the history, physical examination, study of the urine, and cystoscopic and pyelographic investigation.

A careful history and general physical examination should always precede the routine urological investigation, and the results correlated with the findings of urine examination and pyelography. Careful bimanual palpation is of the greatest importance. Palpation of these tumors is sometimes very difficult, but in the hands of experienced examiners a mass in the flank can be felt in a high percentage of the cases.

Cystoscopy, especially when performed at the time of hemorrhage, may show blood coming from the ureteral orifice of the side of the mass. Cystoscopy also enables one to determine the function of the opposite kidney, a factor of greatest importance when operation must be considered.

The flat film may show enlargement of the kidney and distortion of its outline suggestive of tumor.

Retrograde pyelography is our greatest aid in the diagnosis of both benign and malignant renal tumors. Pelvic and calyceal deformities, which in early cases may be very slight, are more clearly shown by this method than by excretory urography. The latter is of value primarily

as a corroborative procedure. Excretory urography is the best means of visualizing the renal contour, and is useful in diagnosing small tumors that cause bulging of the kidney outline but do not produce recognizable deformities of the pelvis and calyces. Used in conjunction with retrograde pyelography, it is frequently very helpful.

The pyelogram may give strong evidence of tumor of the kidney, or it may be unconvincing. In no way can the roentgenographic findings be regarded as characteristic. Renal cancer follows no set rule, and the only consistency of its pyelographic manifestations is their inconsistency.

The following are the most common x-ray findings: (1) enlargement and distortion of the kidney shadow; (2) obliteration or abbreviation of the major or minor calyces or both, or elongation with narrowing (less often with dilatation) of one or two of the major calyces (due to pressure or invasion of the calyces by the tumor); (3) filling defects of the renal pelvis (due to invasion of the pelvis by the growth); (4) displacement of the pelvis laterally, medially, downward, or, rarely, upward; (5) displacement of the ureter medially or laterally (in the case of large growths). The relatively common "spider-leg" deformity results from compression of the pelvis by the mass. Shortened and irregularly dilated calyces, instead of elongated, narrowed, and tapering calyces, is suggestive of the presence of alveolar carcinoma. A large tumor may be present at the lower pole without pyelographic changes, or with minimal changes. Tumors at the more hemmed-in upper pole usually cause renal displacement and calyceal distortion at an earlier date.

Early cases, in particular, require very careful correlation of roentgenographic findings with the patient's history. In doubtful cases, repeated pyelography may be necessary, and, if positive findings persist, exploratory operation should be done.

Any of the pyelographic findings noted above may be caused by other renal or extrarenal lesions. The conditions most likely to cause confusion are polycystic disease (when there is marked deformity of more than one calyx), solitary renal cyst, carbuncle, cortical or perinephritic abscess, tuberculosis, non-opaque stones, and retroperitoneal tumors. Adrenal tumors displace the kidney but do not usually encroach upon the pelvic and calyceal outline, nor do they cause hematuria.

It is seldom possible to demonstrate clinically the type of tumor present in the parenchyma of a given kidney; nor is it always possible to distinguish between pelvic and parenchymal growths.

When the diagnosis of renal tumor in one kidney has been established,

the question of operability must be decided. In this connection, the two most important points to be determined are: (1) the presence or absence of metastases, and (2) the function of the opposite kidney. The latter usually has been ascertained at the time of cystoscopy. The detection of metastases requires roentgenological examination of the lungs and bones.

Prognosis. The prognosis of renal tumors is poor. Without surgical intervention, a fatal outcome is inevitable. In cases seen before metastases are present, surgical extirpation offers a distinct hope of cure. Unfortunately, the majority of the cases are seen late in the disease, when the malignant process has spread beyond the confines of the kidney. The prognosis is directly dependent upon early diagnosis and the complete removal of the tumor before metastases have occurred; yet the early symptoms of renal tumor are so insidious that they are more than likely to be overlooked.

To date, both the immediate and remote results of surgery have been most disappointing. At present, however, surgery offers the best—and perhaps the only—chance for a cure, and should be done at the earliest possible moment. Even though the results have been far from brilliant, one occasionally obtains a cure—frequently where it is least expected.

Treatment. Prompt nephrectomy is the treatment of choice for renal tumor occurring in adults. Radiation, though valuable as an auxiliary measure, is not curable and cannot supplant surgical removal.

The radiosensitivity of tumors of this group appears to vary widely. With the exception of tumors of the Wilms' type, which are known to be relatively radiosensitive as a rule, we have no definite knowledge of the radiosensitivity of parenchymal growths. In the past, deep x-ray therapy has been reserved for palliative treatment of inoperable advanced tumors, usually with extensive metastases, and for postoperative treatment—the latter in the hope that it will devitalize any cancer cells that may have been left behind, thus preventing local recurrence and metastasis. Recently, many urologists and roentgenologists have adopted preoperative irradiation in the treatment of parenchymal tumors, on the grounds that it causes regression of large growths and facilitates operation, controls hemorrhage, and minimizes metastasis. That preoperative irradiation causes temporary regression of huge growths in some instances, thereby rendering them operable, is proved. However, its routine employment as a preliminary to nephrectomy hardly seems justifiable, since the necessary delay results in the loss of valuable time

and may permit metastases to occur. We feel that prompt nephrectomy is still the treatment of choice, and should be done (1) whenever the general condition permits, (2) when there is no evidence of metastases, and (3) when there is no marked functional impairment of the opposite kidney. Slight hypofunction of the other kidney is not usually regarded as a contraindication to surgery since, without nephrectomy, the course of the disease is always fatal. The operability of the tumor itself can usually be determined only after exposure of the kidney.

Irradiation of inoperable tumors, though of palliative value, has not effected permanent cure.

When performing nephrectomy for renal tumor, a wide exposure is necessary to avoid trauma to the vena cava and pleura. Occasionally, in cases of very large growths, adequate exposure may best be obtained by means of the transperitoneal route. Nephrectomy by the abdominal approach has, however, a higher mortality. As a rule, the usual retroperitoneal lumbar incision can be extended sufficiently to remove even very large growths. Some surgeons prefer to tie off the renal vessels through a transperitoneal incision and remove the kidney through the loin. This has not often been found necessary in our experience, the enlarged lumbar incision sufficing in most cases. The success of operation depends upon adequate exposure of the kidney and gentle manipulation, a minimum amount of trauma, and early ligation of the pedicle to prevent the introduction of cancer cells into the blood stream. Preliminary to nephrectomy, it is often advisable to give a blood transfusion since marked anemia is frequently present. Following nephrectomy, deep x-ray therapy is advisable to lessen the risk of metastasis and local recurrence.

The operative mortality of nephrectomy performed for renal cancer is much higher than that of nephrectomy done for other renal lesions. Mathé, in a review of published statistics in 1937, found the mean mortality to be about 19 per cent. *The technical difficulties encountered in the removal of large carcinomas greatly influence the immediate mortality.* Shock, hemorrhage, thrombus-formation due to cancerous cells breaking off and entering the blood stream by way of the renal vein, and cardiac failure due to toxemia produced by infection and by the absorption of degenerating tumor are the chief causes of the high operative mortality.

Heminephrectomy is indicated in cases of tumor limited to one-half of a horseshoe kidney or to one portion of a bifid kidney.

Benign cortical tumors, if small and of unquestionable diagnosis, as

proved by frozen section in the operating-room, may be resected. If large enough to compress the kidney or the adjacent organs, nephrectomy is advisable.

Tumors of the Adrenal Gland

Structure and Function of the Adrenal Gland. The adrenal, one of the glands of the endocrine system, is a small, flattened structure (about 2.5 cm. in diameter) situated just above the kidney on each side. It consists of a thin but firm fibrous capsule, and a cortical and medullary parenchyma. Between the capsule of the adrenal and the kidney is a layer of loose connective tissue, making separation of the kidney from the adrenal in nephrectomy easy. Both the kidney and the adrenal lie within the perirenal fascia. The adrenal is supplied with blood by a superior adrenal branch from the inferior phrenic artery, a small direct branch from the aorta, and an inferior adrenal branch from the renal artery.

The cortex and medulla develop from two separate fundaments. Though united to form a single body, they remain separate and distinct structurally and functionally. The cortex is derived from the mesoderm and, embryologically, is allied with the gonads and other urogenital organs. It elaborates a hormone which is essential to life. The chromaffin cells comprising the medulla are derived from the ectoderm, and have a common origin with cells comprising the sympathetic nervous system. The medulla elaborates an internal secretion called adrenalin or epinephrin.

The correlation of cortical and medullary activities, as well as the complex relationship between adrenal function and that of the gonads and other endocrine glands, is but poorly understood. Cortical hyperactivity produces certain forms of pseudohermaphroditism (female), sexual precocity, and hirsutism. Hypoactivity results in infantilism and asthenia in early life. In postpubertal life, it produces amenorrhea and frigidity in the female, and impotence, obesity, and senilism in the male. Hyperactivity of the medullary tissue produces certain types of paroxysmal hypertension. Insufficiency of the adrenal, as a whole, results in Addison's disease.

Tumors and hyperplasia are the chief lesions which affect the functions of the adrenal glands and their secretions. Tumors of the connective tissue are very rare. The clinically important tumors are those arising from the cortical and medullary cells.

Tumors of the Adrenal Cortex. Primary tumors of the adrenal cortex

are rare, but are of great clinical interest because of the constitutional manifestations which they produce. These appear as various alterations in the secondary sex characteristics and in metabolism.

Pathology. Ewing has classified cortical tumors as (1) hyperplasias, (2) adenomas, and (3) carcinomas.

Hyperplasia occurs fairly often in adults. It may be nodular or diffused. The nodules vary from pinhead to pea size. This type is sometimes difficult to distinguish from small adenomas. Sometimes the cortex shows diffuse hyperplasia, with great enlargement of the adrenal gland; this form gives rise to a clinical picture similar to that produced by cortical neoplasms.

Adenomas are the most frequent tumors of the adrenal cortex. They vary in size from a few millimeters to 10 or 12 cm. in diameter, are of a mottled brown and yellow color, and are often encapsulated. They rarely give clinical indications of their presence unless they attain a large size, when they may induce hyperadrenalism. As a rule, they remain small, and are usually discovered accidentally at autopsy. They are frequently bilateral. Geschickter states that the distinguishing characteristics of the adenomas are the definite cortical cells, tendency to lipoidal degeneration, marked capillary network, pigment deposits, and the arrangement of the cells in cords and bundles. Larger ones are distinguished by areas of vascularization. A feature which distinguishes these adenomas from the so-called hypernephromas of the kidney is the absence of tubular or papillary structures.

Carcinomas of the adrenal cortex are rare. In a series of 105 cases of adrenal tumor reviewed by Geschickter, 72 were cortical tumors, of which only 6 were malignant. These tumors are extremely rare in children. Malignant cortical tumors are usually soft growths of a yellowish color and a varied consistency. They have a tendency to hemorrhagic and necrotic areas, and to cystic degeneration following necrosis. These tumors metastasize early and widely through the lymphatics of the venous system, most frequently to the liver and lungs, and but rarely to the bones. Occasionally they metastasize to the opposite adrenal gland. Invasion of the kidney, and of the renal vein and vena cava, by direct extension, is common.

Tumors arising from adrenal rests occasionally occur in various parts of the body, particularly the liver, kidney, testis, broad ligaments, and retroperitoneal tissues.

Symptoms. Cortical adrenal tumors may or may not produce clini-

cally apparent endocrine changes. Langeron and Loheac have classified these tumors according to symptoms, as follows:

- (1) Tumors presenting an endocrine syndrome
- (2) Tumors with only an abdominal mass
- (3) Tumors with metastatic masses
- (4) Tumors with arterial hypertension (paroxysmal or continuous)

The clinical evidence of tumors of the first group may be (a) hypoadrenalism (in early life, infantilism; postpubertally and later, impotence, sterility, adiposity, amenorrhea, frigidity); (b) the adrenogenital syndrome of adrenal virilism (sexual precocity and premature maturity in both sexes, and, in females, masculinity, hirsutism, etc.). Cahill states that the tumor which produces the endocrine changes has cells resembling the reticulate layer of the adrenal gland, and has an increase in fuchsinophilic granules over normal; the adrenal cortex hormone has not been demonstrated in these growths. This type of tumor appears more frequently in females. The tumor without endocrine syndromes has cells resembling more the fasciculate layer of the adrenal and containing only small amounts of fuchsinophilic granules.

When congenital, the tumor results in pseudohermaphroditism (female).

When the tumor occurs before puberty in the male, the most frequent change is premature puberty. There is rapid physical development, with adult type of genitals and distribution of hair, and development of sexual desire. In female children, such tumors most frequently cause prematurity with masculinizing alterations. Changes in the genitals may vary from slight to marked. *There is no normal development of the breasts.* Menstruation, as a rule, does not take place.

Postpubertal tumor, in the male, may cause inversion changes toward femininity (hypertrophy of the mammae, atrophy of the testes, adiposity), but these are much rarer than inversion changes in the female. The usual symptoms are the presence of a tumor in the abdomen and weakness. In the female, when tumor occurs after puberty and before the menopause, there is very frequently suppression of femininity with alterations toward adult masculinity: amenorrhea, with loss of sexual desire and libido, hirsutism, deepening of the voice, and adiposity. In more malignant tumors, there is emaciation instead of obesity.

In the second group—those with an abdominal tumor only—the symptoms are those due to pressure on or displacement of adjacent viscera.

The third group—metastatic tumors—give infinitely varied symptoms, according to the location of the metastases.

The fourth group is the least understood. In this group are various disturbances of metabolism resembling those described by Cushing and assumed to be associated with basophilism: duskiness and redness of the face and hands, dryness and coarseness of the skin, excessive growths of hair, adiposity, accompanied by hyperglycemia. Occipital headaches, weakness, and palpitation of the heart are common complaints. Symptoms of hypertension are frequent; such hypertension is likely to be continuous rather than paroxysmal, as in medullary tumors. These metastatic disturbances may be present with or without changes in the secondary sexual characteristics.

Diagnosis. The adrenogenital syndromes are not pathognomonic of adrenal tumor, since these changes also occur with hyperplasia of the adrenal cortex, and somewhat similar changes are seen in the presence of tumors in other hormonal glands—particularly basophilic adenomas of the pituitary and certain tumors of the ovary and testis. Adrenogenital syndromes appear more frequently without any demonstrable tumor, and hyperfunction of the adrenal cortex has been assumed to play a part in their production (Cahill; Broster and Vines).

In a thin person, a tumor may often be felt, or downward displacement of the kidney may be palpated.

The tumor may show as a soft tissue mass in the roentgenogram, and renal displacement or rotation may be revealed by means of a pyelogram. Roentgenography following injection of air into the perirenal fascial planes, as advocated by Carelli and modified by Cahill, may outline the tumor.

Prognosis. If discovered sufficiently early, removal of the adrenal containing a tumor will not only save the patient's life but will produce a symptomatic cure of the endocrine disturbances, though the fixed anatomical changes are not corrected. Unfortunately, adrenal tumors that do not produce endocrine syndromes seldom give early manifestations by which they may be distinguished. Only when the tumor has reached a large size, and gives pressure symptoms, is it discovered as a rule, and by that time irreparable damage has frequently been done. Metastasis of adrenocortical tumors produces the same endocrine alterations as the original growth.

Treatment. Treatment is surgical removal of the adrenal. A transperitoneal approach, through an oblique subcostal incision, permits exploration of both adrenals. Cahill advises this procedure, as it permits ligating the vessels, especially the veins, before the tumor is manipulated, thus preventing possible metastases from that cause, as well as the possi-

bility of large amounts of adrenal secretion being injected into the circulation. To the latter has been attributed the collapse that immediately follows adrenalectomy in a certain percentage of cases.

The extraperitoneal lumbar approach, with the posterior angle of the incision extended higher on the back, gives good exposure of the adrenal but does not permit simultaneous exploration of both adrenals—a very important point. Some surgeons prefer bilateral exposure of the adrenals to determine the diseased side and the condition of the opposite adrenal.

Exploratory operation is indicated whenever the diagnosis is in doubt.

The best and most complete exposition of the adrenal glands and their treatment that has come to our attention is that of Dr. Hugh H. Young, contained in his book *Genital Abnormalities, Hermaphroditism, and Related Adrenal Diseases*, and to this excellent résumé of the subject we refer the interested reader.

Tumors of the Adrenal Medulla. Tumors arising from the adrenal medulla are rare, extremely malignant, have an irregular, rapid course, and metastasize extensively. In general, the patients manifest signs and symptoms indicating instability of the sympathetic nervous system.

Pathology. Three main types of adrenal medullary tumors have been distinguished.

Neuroblastoma (medulloblastoma) develops from the primitive undifferentiated neuroblast. These tumors are rapid-growing and highly malignant. They extend early to both sides of the spine, and produce extensive metastases throughout the body. The metastases show soft tumor masses similar to the primary growth. The latter is usually reddish or reddish-brown in color, well encapsulated, and is often firm and nodular in consistency, though it may be soft and spongy. It usually depresses the kidney on that side, but does not invade it. On microscopic examination, the neuroblastoma may show cells of the sympathetic series in various stages of development (sympathogonia, sympathoblasts, or neuroblasts). By far the most frequently seen cell is slightly larger than a lymphocyte, with a minute amount of slightly basophilic and finely granular cytoplasm; this is a rapidly multiplying, highly embryonic, undifferentiated round cell. The cells are embedded—often in pseudorosette formation—in an intercellular substance consisting of a very fine network of minute fibrils. Hemorrhage, often massive in type, and necrosis are very common findings. Direct extension to neighboring viscera frequently takes place—sometimes before distant metastases are observable.

Two entirely different clinical syndromes have been described in

connection with these tumors, according as the right or left adrenal is the site of the primary growth, and according to the location of metastases. Tumor of the left adrenal gland is identified with the so-called Hutchison type of metastases (to the skull, usually with metastatic involvement of the orbit). Right-sided tumors give rise to the Pepper type of metastases (extensive involvement of the liver and retroperitoneal lymph nodes). The location of the metastases is explained by the arrangement of the lymphatics on the two sides. The left lymphatics are connected with lumbar glands and pass downward to the groin and aortic glands, and upward to the deep cervical glands and to the skull. Those from the right adrenal empty directly into the portal system, and the right adrenal gland lies in direct contact with the liver. At present, there is great doubt entertained regarding the justification and value of these syndromes. Patients presenting the clinical features of the Pepper type will usually be found to have neuroblastoma originating in the right adrenal; but in those presenting the Hutchison type of metastases the primary tumor originates almost as often from the right as from the left adrenal. Moreover, both of these syndromes may occur with other tumors of the adrenal and of the kidney.

Ganglioneuroma develops from the mature sympathetic ganglion cell. It is very rarely found in the adrenal medulla. It may be discovered as a small growth at autopsy, or it may enlarge sufficiently to cause pressure symptoms and thus be discovered clinically. The structures show a preponderance of medullated and non-medullated nerve fibers, among which lie groups of more or less well-formed proliferating ganglion cells (Alyea). The tumor is usually single, but may be multiple. It is almost always benign. When malignancy is present, its degree depends on the relative proportion of mature and immature cells. The more mature the cell, the greater the malignancy.

Pheochromocytoma (paraganglioma or chromaffinoma) of the adrenal is a rare, soft, very red tumor, which is usually solitary and benign. As a rule, these tumors are small, but they may reach a considerable size. Belt and Powell reported a cystic chromaffinoma weighing 1,000 Gm. which had replaced the right adrenal gland.

Symptoms of Medullary Tumors. These patients show signs and symptoms indicating instability of the sympathetic nervous system: paroxysmal hypertension; glycosuria; vasoconstriction and vasodilatation of the peripheral vessels, indicated by pallor and sweating; headache, nausea, and vomiting. They manifest an unusual susceptibility to

surgical shock. In addition to the above symptoms, there are local symptoms due to the growth itself.

Diagnosis. The diagnosis of medullary tumors of the adrenal is based on the history, physical examination, and x-ray examination.

Prognosis and Treatment. The ultimate prognosis of the malignant tumors is hopeless, due to the bigb malignancy of the primary tumor, the rapidity of the course, and the extensiveness and malignancy of metastases. Neither surgery nor roentgen therapy has been of much avail.

Aneurysm of the Renal Artery

Aneurysm of the renal artery is a rare condition. Medical literature contains reports of only 75 cases. Mathé, in 1932, wrote an excellent review of the subject and collected 55 cases from the literature. Lowsley and Cannon, in 1942, tabulated 20 cases reported since Mathé's exhaustive review, and added 1 case seen at the Brady Foundation.

Renal aneurysm may occur at any age, and is somewhat more prevalent in males.

Etiology. Trauma—to the loin, back, or upper part of the abdomen—usually given as the chief etiological factor, probably does not of itself cause aneurysm, but may readily be the impetus for an aneurysmal dilatation in a renal artery that is already weakened by congenital defect (especially at its bifurcation), vascular disease, or infection.

Pathology. Two fundamental factors underlie the development of an aneurysm of the renal artery, namely: (1) the arterial wall is weakened by congenital defect, trauma, or disease (arteriosclerosis, periarteritis nodosa, syphilis or other infection); (2) the pathogenesis is directly related to intrinsic and extrinsic vascular pressure.

Renal aneurysms are classified as *true* and *false*. True aneurysms are saccular or fusiform dilatations of the arterial wall itself. They are usually small, ranging from the size of a pea to that of an orange, and often show calcareous deposits which are opaque to the x-rays. So long as true aneurysms remain unruptured, they are unlikely to produce any definite symptoms. Pressure and occlusion of the aneurysm may cause thrombi and infarcts of the renal parenchyma.

False aneurysms are formed as the result of trauma, disease, indirectly by the rupture of a true aneurysm, or directly by the rupture of the renal artery. They are larger than true aneurysms, the smallest in the reported cases measuring 10 cm. by 15 cm., and the largest filling one-half of the

patient's abdomen. The wall of a false aneurysm is composed of condensed fibrous tissue developed around the extravasated and coagulated laminated blood. A false aneurysm may extend into the retroperitoneal space, rupture, and form a large hematoma; or it may rupture into the peritoneal cavity or into the renal pelvis, sometimes causing death by exsanguination. Blood may distend the pelvis and calyces and produce complete absorption of the renal parenchyma; or atrophy of the kidney may result from extravasation of blood within the capsule. The blood clot may displace and become firmly matted to the neighboring organs.

Symptoms. Small true aneurysms seldom present symptoms, and usually are discovered accidentally during investigation of the kidney or at autopsy. A few patients have complained of pain in the flank. The cardinal signs and symptoms of a false or a ruptured aneurysm are pain, tumefaction, and hematuria. As a true aneurysm increases in size, or ruptures spontaneously or traumatically to form a false aneurysm, it gives rise to a tumor mass in the flank or upper abdomen. This tumefaction may develop suddenly, or over a period of months. The mass is usually smooth, firm, somewhat tender, and fixed in position. A systolic bruit, when present, is pathognomonic. Hematuria occurs when the aneurysmal sac has ruptured into a calyx, or the renal pelvis, and may be so extensive as to cause death. Hematuria in cases of true aneurysm is the result of renal thrombi and infarction.

Diagnosis. The clinical diagnosis of renal aneurysm is difficult, and was made in only 12 of the 75 reported cases. Calcific deposits in the wall of the aneurysmal sac appear, in the x-ray film, as a ring-like shadow in the region of the kidney or the renal hilum; and in 3 cases, including the one seen in our service, the diagnosis was made on the roentgenographic finding of such a ring-like shadow with a dense periphery, disrupted in one portion, and a rarification of the center. While suggestive of calcified aneurysm, this shadow must be differentiated from that cast by a gallstone, renal calculus, calcified lymph gland, calcified cyst, and calcification in neoplasm and tuberculosis.

False aneurysms offer a particularly perplexing diagnostic problem. While traumatic rupture of a false aneurysm, or spontaneous perforation of a true aneurysm, is to be considered in the presence of intermittent hematuria associated with severe lumbar pain and a rapidly or slowly enlarging, fixed, tender swelling in the flank, this syndrome may also be presented by a ruptured kidney, so that clinical differentiation may be impossible. In unruptured false aneurysm the most valuable signs are

tumefaction and a systolic bruit. The latter, however, has been present in only a few cases.

Treatment. Symptom-producing aneurysms that are not operated upon inevitably prove fatal. Death may occur a few hours or several years after the onset of symptoms, but in most of the published cases the patients died within a year of the appearance of symptoms—usually from exsanguination from hemorrhage caused by rupture of the aneurysm into the renal pelvis, peritoneal cavity, or retroperitoneal space.

A suspected or roentgenographically diagnosed renal aneurysm therefore demands immediate surgical investigation, and, if the diagnosis is confirmed, nephrectomy. The latter has proved curative in 26 of the 29 cases in which it has been done, and is indicated even in small true aneurysms, with mild or no symptoms, because of the ever-present danger of rupture and hemorrhage. Exposure of a pulsating aneurysmal sac or perirenal hematoma must be done with the utmost caution as the slightest tear in the sac may result in severe hemorrhage. If the tumor is large and hemorrhage appears inevitable, the friable pedicle should be approached transperitoneally and clamped near its branching from the aorta.

Renal Calculus

Urinary lithiasis constitutes one of the chief problems of urology. The more recent urological literature contains many contributions relating to calculous disease, particularly its etiology and prevention. Pains-taking research on the part of numerous investigators along the lines of bacteriology, chemistry, and body metabolism has resulted in greatly augmented knowledge of this phase of the subject, much of which, however, must still be regarded as theoretical.

Though the cause of their formation is still uncertain, the effects produced by the presence of stones in the urinary tract have been only too well demonstrated. Unless passed or properly removed, the frequent complication of obstruction-infection eventually results in irreparable destruction of renal tissue.

The majority of urinary calculi originate in the kidney. A certain number remain attached to a papilla, or in a calyx, or in the renal pelvis, where they gradually increase to a size which prohibits their passage into the ureter. Retained here, the stone presents the problem of renal calculus. Commonly, however, while still small the stone passes into the ureter; either it is evacuated spontaneously or retained in the ureter,

or lower down, in the bladder or urethra (Ureteral Calculus, p. 1259; Vesical Calculus, p. 1067; Urethral Calculus, p. 665). Stones also form primarily in the bladder, and under conditions of stasis may originate occasionally in the ureter and urethra, but there is little doubt that most calculi found in these portions of the tract descend from the kidney.

Incidence of Renal Calculus. Renal calculus occurs at all ages, but commonly between the ages of 25 and 40 years. Stone seldom begins to form in the kidney after the age of 50 years, and stones in the kidneys and ureters of children are uncommon. Joly found renal lithiasis to be "a disease of middle life, over 50 per cent of the total number of cases being between the ages of 30 and 50." In making any statement in regard to age incidence, one must remember that stones frequently grow so slowly or are so located that they cause no symptoms, and therefore may have existed for many years before being diagnosed.

Males appear to be more subject to renal stone than are females. In our own series, the proportion of males to females has been approximately 3 to 2. In numerous other reported series, however, the percentage of males has been only slightly higher than that of females.

Both kidneys are affected about equally. A study of the literature indicates that the stones are bilateral in from 10 to 20 per cent of cases, although several authors have raised this figure to 25 per cent and even higher. The stones are multiple in approximately 40 per cent of cases. Multiplicity is much more common in bilateral cases (60 to 65 per cent). Bilateral and multiple stones are frequently associated with infection and obstruction.

Etiology. The mechanisms of the formation of renal stones and the factors which initiate these mechanisms are unknown. Prominent among the many etiological theories that have been advanced are colloid-crystalloid imbalance, stasis, infection, vitamin-A deficiency, endocrine disturbances, heredity, racial predisposition, and climate. Several concurrent factors are probably always required for the formation of a renal stone rather than any single factor. "No stretch of chemical or physiological imagination will permit so heterogeneous a group of compounds to be ascribed to a common origin, or their deposition, in kidney, ureter or bladder, to be uniformly charged to an identical cause." (Howard Kelly)

Colloid-Crystalloid Imbalance. Much importance has been attached to colloid-crystalloid imbalance as a cause of renal stone—a theory propounded many years ago. The urine is a supersaturated solution, and

the crystalloids are held in solution because of the presence of protective colloids; but when there is an increase or diminution in colloids or crystalloids the result is an imbalance, with a subsequent precipitation of one or the other and organization into stone. Keyser was able to produce urinary stones by causing such an excessive secretion of crystals in the urine that the protective colloids were no longer able to hold the crystalloids in solution, and the latter being insoluble in urine, crystallization into stone resulted. Infection, an error in metabolism, or anything which disturbs the colloid-crystalloid equilibrium of the urine will result in the precipitation of urinary salts, and this precipitation, even though it be very slight, may act as a nucleus for the formation of a stone. An excessive amount of crystalloids in the urine may be present, however, without stone developing (*i.e.*, phosphaturia, cystinuria, and oxaluria).

Stasis. The theory that stasis in the urinary tract predisposes to stone is a very old one. Urosthesis associated with infection is undoubtedly responsible in some cases for the formation of renal calculi. There is little evidence, however, that stasis can of itself initiate the stone-forming process. We quote Keyser:

Experimentally, the production of urosthesis *per se* almost never leads to calculosis. Stasis in itself is not a cause. However, when the stone-forming mechanism is present, when crystals are being so deposited by infection or colloidal disturbances that they tend to fuse, it can be easily understood how stagnation enhances their retention and growth.

Calculi have been found relatively more often in kidneys subject to some interference with drainage, either anatomical, mechanical, or pathological. An embryonic stone, which ordinarily would pass down the ureter to be evacuated in the course of micturition, may, in one of sedentary habits or with an elongated calyx or other slight anatomical abnormality, be retained in the renal cavity, where it gradually enlarges. Faulty drainage of the kidneys probably accounts, in part at least, for the relative frequency of renal stones (often bilateral) in patients who have been immobilized in bed for long periods of time because of fractured bones, osteomyelitis, cord injuries, or systemic disease. When an individual is kept on his back, drainage from the renal pelvis and calyces is more or less impeded, for the highest point will be the ureteropelvic junction. If a deposition of crystal does take place, it may be retained as the nucleus of a calculus because the force of the urinary stream is not sufficient to wash it away. This may take place in any of the calyces, thereby differing from stone-formation in ambulatory patients, in whom

the stones are usually found in the pelvis or lower calyx—rarely in the upper half of the kidney. Other factors which must be considered in these cases are infection and loss of calcium during long periods of complete muscular inactivity.

Although stasis is undoubtedly a factor in some cases of renal stone, it is not in itself a cause. In many cases of renal calculus, obstruction and stasis are absent.

Infection. The role played by infection in the production of renal stone is uncertain. There can be no doubt that it is an important etiological factor in a certain number of cases. On the other hand, there are many cases of renal stone without infection. Moreover, a majority of renal infections are due to the colon bacillus; the larger number of these are not associated with stone.

Many years ago Albarran divided renal calculi into primary stones (without infection) and secondary stones (in association with some urea-splitting organism). Since then, many theories have been advanced as to the part which infection plays in the formation of urinary calculi. Rosenow and Meisser (1922-23) presented their views as to the importance of focal infection in the genesis of urinary lithiasis, and demonstrated a specificity of certain strains of bacteria, especially streptococci, in the formation of stones. They inoculated the pulps of the teeth of previously healthy dogs with streptococci isolated from the urine, teeth, and tonsils of 9 patients afflicted with recurrent nephrolithiasis, and succeeded in producing calculi or medullary lesions in 87 per cent of the animals. The experimentally produced calculi were similar in physical properties and chemical composition to those found in nephrolithiasis in man, the number and size of the stones being often in proportion to the length of time the experiment was allowed to continue.

The literature provides abundant clinical evidence that renal stone-formation is associated with specific alkaline and urea-splitting streptococci, staphylococci, and proteus organisms. Hagar and Magath (1926) demonstrated that certain stones form in the presence of the *Bacillus proteus*. Later investigation has proved not only that this organism has definite stone-forming qualities by virtue of its urea-splitting properties, but that the infection it produces is extremely difficult to eradicate. The streptococcus is not often found alone in ureteral calculus, but it may be discovered in association with various other bacteria. When this occurs, the presence of streptococci invariably increases the virulence of the infection, thus giving a graver prognosis. Pyogenic staphylococci

have been unquestionably demonstrated to be frequently associated with secondary stone-formation. A clump of cocci may act as a foreign body, upon which insoluble salts are deposited until a calculus is built up. Hellström found staphylococci in all layers of calculi which he dissolved in hydrochloric acid and stained. Albus was seen most frequently, usually being found alone; but in some cases where only bacilli had been isolated from the urine, cocci were found in calculi taken from the same patient. Cahill names, as the second of the three main factors in the production of renal calculi, "infection by bacteria with the power of splitting urea, particularly staphylococcus and proteus" In the opinion of Joly, it is not to be assumed that either *Bacillus proteus* or any cocci have especial lithogenic powers; "they merely create conditions which are peculiarly favorable for stone-formation." This author, whose experience with urinary lithiasis has been extensive, states that calculus-formation following a pure colon bacillus infection is very rare, though mixed infections of coliform bacilli and pyogenic cocci are frequent. In these mixed infections, he believes, the coccal infection is the primary one and certainly the more important.

According to Randall, infection plays an important role in the production of renal stone by causing minor papillary lesions or injuries to the linings of the calyces of kidneys otherwise normal. These infection-induced injuries constitute focal points where the crystallization of urinary salts may be initiated, and a true "primary" renal stone thus brought into existence.

When we add to these possible factors in the field of infection the possibilities of circulatory troubles, of metabolic diseases, and of allergic reactions, it seems safe to surmise that pelvic lesions do, and must occur in greater frequency than at present suspected. . . . The hypothesis offered is that upon such a lesion crystallization of a "primary" renal calculus first takes place, and that its chemical character depends upon the salt in the urine, which at that epoch is the most supersaturated one.

Randall thus includes in a broad conception not only the infection theory of causation but several of the newer theories, such as deficiency in vitamin A, so that he does not regard renal calculus as a disease entity *per se* but, rather, as the symptom of certain abnormal conditions within the body. This, in general, is the attitude of the majority of urologists at the present time.

In recurrent nephrolithiasis, at least, persistent infection, with or without stasis, is a very important etiological factor. Rovsing (1924)

investigated 109 cases of recurrent nephrolithiasis and found 71 per cent of all recurrences in kidneys infected primarily or secondarily with urea-decomposing organisms. Keyser noted that recurrent phosphate and carbonate stones are often associated with infections of coccic or bacillary type. In a study of 44 cases of recurrent calculi following operations for nephrolithiasis at the Brady Foundation, of the New York Hospital, Twinem (1937) found the colon bacillus in the largest number of cases, with the *Bacillus proteus* second, and staphylococci third. In the 10 cases of most frequent recurrence, the *Bacillus proteus* was found in 6 cases, staphylococci in 2, *Bacillus lactis aerogenes* in 1, and *Bacillus proteus* and *Bacillus fluorescens* in 1. Multiple calculi also occur more often in the presence of urinary infection.

It must be admitted that despite much experimental work and clinical observation, the relation of extrarenal and local urinary infections to the formation of renal stone remains uncertain. Nephrolithiasis in association with urinary infection is of very frequent occurrence. On the other hand, aseptic stones are common. So, also, are urinary infections without stone. It would appear, therefore, that while it undoubtedly often influences the occurrence and character of renal stones, infection, like stasis, is not an essential prerequisite to their formation.

Metabolic and Endocrine Disturbances. VITAMIN-A DEFICIENCY. Dietary and hygienic conditions are important factors in stone-formation. Improved living conditions and, particularly, improvement in the quantity, quality, and variety of food, have resulted in a gradual but definite decrease in the number of cases of urinary stone.

Clinical observations have clearly indicated that there is a direct relation between stone-formation and the absence of certain essentials from the diet. Definite stone areas have been found to exist in India, the southern part of China, Egypt, Mesopotamia, Derbyshire and Westmoreland in England, the southeast of France, the Volga Valley in Russia, and in Dalmatia. Many theories have been advanced to account for this geographical distribution of lithiasis. Geographical studies of urinary stone show that it is relatively uncommon in dairy-farming countries, such as Switzerland, Denmark, and Ireland, and where the population is able to enjoy a well-balanced and mixed diet, and that it is most prevalent in people living on a monotonous diet, particularly where cereals form the staple food.

That lithiasis is a deficiency disease is borne out by the notably decreased incidence of urinary stone—particularly bladder stone—in civi-

lized countries in childhood since the institution of modern diets which prevent avitaminosis. Vesical stone, which once was very common in both European and American statistics, now is a rare disease. However, in parts of India and China where living conditions and dietary standards have not changed, vesical stone is still exceedingly common. Fresh vegetables, milk, and cod-liver oil have probably contributed more than any other factors to this lessening of the incidence of urinary stone in childhood.

For centuries it has been assumed that climatic conditions, racial predisposition, and heredity powerfully influence stone-formation, directly or indirectly. Renal stone is much more common in warm countries than in cold, and in the dry tropics than in the wet. In Ecuador, for example, stone, is almost unknown, whereas in Mesopotamia calculous disease is exceedingly common among the natives. This difference in the incidence of lithiasis in the wet and the dry tropics is now believed to be due primarily to dietary factors and only secondarily to climatic conditions. In the wet tropics, the native diet is usually rich in vitamins. Joly states in this regard:

Dry heat acts simply by diminishing the quantity of urine eliminated, and so increasing the concentration. If the colloid mechanism by which the stone-forming salts are kept in solution is defective, they will tend to be precipitated in the urinary passages and may give rise to stone-formation. This, however, does not occur in healthy, well-nourished individuals.

Regarding the racial incidence of lithiasis, one is struck by the frequency of stone among the Hindus, Arabs, and Southern Chinese. When the inhabitants of these countries are transported and settled elsewhere, their descendants exhibit the same tendency *provided* they preserve and carry on their tribal and ancestral habits of living and continue to subsist on the same diet. But wherever the general standard of living has been raised, particularly where more and a greater variety of food has become available, there the incidence of renal stone has steadily diminished. The Negro, on the other hand, is almost immune to stone despite the fact that, in Africa in particular, the negro population lacks suitable food and proper sanitation. Originating in an intensely hot climate, the Negro was transferred to the less torrid southern portion of the North American continent, and thence he has travelled northward; but in every climate he has preserved his immunity to renal lithiasis. It has been suggested that the fact that the Negro eats more meat than members of other races of like economic status may be the actual reason for the

"racial" immunity he apparently enjoys. Urinary stone is also extremely rare among the Esquimaux. The consensus of opinion among present-day observers is that the formation of urinary stones is not so much a matter of climate and race as of the food produced in that climate and consumed by that race.

Great stress was formerly laid on the influence of heredity, but with little supporting evidence being adduced. In the so-called stone areas cases of stone have not been found to run in certain families. The only form of lithiasis which is definitely familial is that in which cystine stones are formed.

That a deficiency of vitamin A is a fundamental factor in stone-formation was clearly demonstrated by the experimental work of Osborn and Mendel on rats in 1917. Autopsies on 857 rats showed phosphatic calculi in the kidneys or bladder in 9.3 per cent, and it was observed that "in every instance where calculi developed, the animals were without an adequate source of the fat-soluble vitamin for some time." No other pathogenic factor common to all of the affected animals, which might explain the formation of the urinary calculi, could be found. This apparent relationship between a diet deficient in vitamin A and the formation of stone was confirmed in 1926 by the work of Fujimaki, who found that rats kept on this diet for about 12 weeks always developed phosphatic stones in the bladder and kidney and cholesterol stones in the bile duct. McCarrison, in 1931, showed the keratinizing effect on the epithelium of the urinary tract produced by the lack of vitamin A in the diet, and concluded that desquamated, keratinized epithelium from the urinary organs may serve as the nuclei of stones, which are always formed largely of calcium-magnesium phosphate. He also noted that if the vitamin C factors were also removed, there was still greater likelihood of renal stone-formation; and if, to an individual on such a deficient diet, earthy phosphates were fed, the rapidity with which stones formed was very noticeable. From observations obtained with 84 rats, this author and Ranganathan concluded that the essential factors in the production of stones in rats are (1) a deficiency of phosphate relative to the amount of calcium injected, and (2) an insufficiency of vitamin A in the diet; a balance of calcium and phosphorus will not prevent calculus-formation unless there is a sufficiency of vitamin A. Higgins, during a long series of experiments, found that when rats were maintained on a vitamin-A-deficient diet "42 per cent had renal and 88 per cent had bladder calculi."

Renal Stone Following Treatment of Peptic Ulcer with Alkalis. There is a prevalent belief that patients on a Sippy régime for the treatment of peptic ulcer frequently develop stones. In this régime, large amounts of alkali are given together with high calcium and phosphate diets, resulting in increased phosphaturia and calcinuria with, at the same time, an alkaline urine. Theoretically, under these conditions urinary stones might be expected to form.

In order to determine the etiological relationship, if any, between the use of alkalis in the treatment of peptic ulcer and kidney and ureteral stone-formation, Kretschmer and Brown (1939) made a detailed study of 680 cases of peptic ulcer treated at the Presbyterian Hospital (Chicago). These patients, all of whom replied to a questionnaire, had been treated with alkalis for periods of from 3 to 6 months, averaging 4 months. Many had taken minor amounts for much longer periods. It was found that 21 patients (3.1 per cent) had a history of urinary stone before presenting themselves for the treatment of ulcer, and 33 (4.9 per cent) had stone some time after ulcer treatment—in many instances from 10 to 20 years later. The small difference of 1.8 per cent in the incidence of stone between individuals who were given alkalis and those who were not appeared to the authors to be so insignificant as to make it improbable that alkalis used in the treatment of ulcer play a role in stone-formation. In addition, these authors studied the records of 1,260 cases of renal and ureteral calculi, and found 7 in which the diagnosis of stone and ulcer was made simultaneously and in which there had been no ulcer treatment, and 26 with a previous history of ulcer; of the latter, only 15 (1.2 per cent) had received alkalis. This incidence of only 1.2 per cent of treated ulcer cases in a series of 1,260 renal and ureteral calculi also fails to support the theory that alkalis used in the treatment of peptic ulcer cause renal stones.

Stone-Formation in Hyperparathyroidism and in Immobilized Patients. The recent work of Albright, Aub, and Bauer has shown that in cases of hyperparathyroidism caused by tumor of the parathyroid there arises a disturbance in the calcium and phosphorus metabolism with associated increase of both calcium and phosphorus in the urine. It is believed that this disturbance of the calcium-phosphorus metabolism upsets the colloid-crystalloid equilibrium of the urine, with subsequent precipitation and coalescence of the urinary constituents. This, however, is uncertain. Many patients with hyperparathyroidism develop urinary calculi. Barney and Mintz (1934) reviewed the literature and found 65 cases of

hyperparathyroidism, with renal calculi in 15 (23 per cent); in addition they reported 11 cases of renal stone in 18 cases of hyperparathyroidism observed at the Massachusetts General Hospital (Boston), in which the diagnosis was confirmed by operation. Parathyroid disease, they state, appears to be the causal factor in 10 per cent of the cases of urinary lithiasis.

Because a systemic disturbance is responsible for the calculus-formation, the stones have a tendency to be multiple, bilateral, and recurrent. Surgical removal of the parathyroid tumor will restore the output of parathyroid secretion to its normal amount, and this will result in reduction of the blood calcium and phosphorus, which, in turn, will reduce the excretion of these elements in the urine.

Urinary calculi are often found in individuals suffering from bone injuries, tuberculous hip joints or spines, osteomyelitis, empyemia, or other conditions requiring immobilization for prolonged periods. These calculi are always found in the upper tract and tend to be bilateral.

Immobilization may operate in two ways to produce stones: (1) by impairing drainage, as already noted; (2) by producing changes in calcium metabolism. Jones and Roberts (1934) showed that immobility causes local decalcification of the bones, and demonstrated by x-ray that generalized disuse depletes the calcium store of the whole skeleton. It appears likely that nephrolithiasis in these cases is the result of skeletal decalcification, and is comparable with the stone-formation seen in connection with hyperparathyroidism.

Among the most important recent contributions to this subject are the investigations of Flocks and his co-workers at the University of Iowa.¹ These observers studied the urinary excretion of calcium and phosphorus under fixed conditions in a group of 35 patients known to be suffering from renal calculus; in 23 they found high urinary calcium excretion, while in 3 with low urinary calcium there was a history which suggested that the calcium excretion was probably high at the time stone-formation was initiated. Only 2 patients had clinical evidence of hyperparathyroidism.

These authors consider that two groups of factors are fundamental in the pathogenesis of renal stone: (1) those factors which so change the nature of the renal substance as to favor precipitation of the crystalloids

¹ These valuable contributions to the etiology of renal stone were made available to us through the courtesy of Dr. Flocks and his associates at the College of Medicine of the State University of Iowa, who permitted the use of work as yet unpublished by giving us access to the original manuscript.

within it, and (2) those factors which favor the precipitation of crystalloids in the urinary passageway. In any given patient, either or both groups of factors may operate at the same time or at different times. Stasis, infection, vitamin-A deficiency, hyperparathyroidism—all may play a role in the stone-forming process, inducing precipitation of crystalloids in the renal substance. We quote from Flocks' thesis:

The two fundamental factors determining the precipitation or solution of calcium and phosphorus in the urinary passageways are the urinary pH and the urinary concentration of calcium and phosphorus. Certain accessory factors may also be of importance, i. e., the colloids of the urine, the surface tension of the urine, the presence of stasis, and the presence of bodies which might act as nuclei for the precipitation of the crystalloids. The importance of the hydrogen ion concentration, and the ease with which this concentration can be changed to the alkaline side by urea-splitting organisms, together with the marked frequency with which these organisms occur in patients with renal calculi, has been demonstrated by many workers. Experimentally, the importance of the increased concentration of crystalloids in the urine has been emphasized by Keyser. The high incidence of urinary stone in hyperparathyroidism, where increased urinary excretion of calcium and phosphorus occurs, has been emphasized by Albright and Barney. The high incidence of urinary calculi in patients with bone disease, where presumably there is some alteration in calcium metabolism, probably associated with increased calcium excretion, has been emphasized by Holmes and Coplan, Jones and Roberts, and others. Steiner has demonstrated that the epithelial desquamation which occurs in vitamin-A deficiency may act as a nucleus for the precipitation of crystalloids. Again, there is a multiplicity of factors which may be present in each individual patient.

There are, then, two groups of factors in the pathogenesis of renal stone: first, those factors which are associated with the precipitation of crystalloids in the kidney substance; and second, those which are associated with the precipitation of crystalloids in the urinary passageway . . . increased excretion of calcium and phosphorus in the urine may be of importance in *both* groups of factors. . . .

It would seem that although the high concentration of the calcium in the urine of itself is not enough to bring about precipitation in the kidney substance, or in the urinary passageway, it would predispose these individuals to this occurrence. Therefore, given a patient or individual with a high urinary calcium, other factors being equal, he would be more likely to form stone than one with a low urinary calcium.

By comparing the function and roentgenographic appearance of the two kidneys—one with stones and the other normal—in the same individual, these investigators determined that slight pathological changes are usually associated with a definitely increased calcium value in the urine from the affected kidney, as compared with the output of its normal mate; but when the affected kidney showed marked pathological change, its urinary calcium was usually definitely lower than that excreted by its normal mate.

Calculi Due to Sulfonamide Therapy. In recent years numerous cases of urinary calculi due to the administration of the sulfonamide drugs have been reported. Crystals of these drugs are excreted in the urine, and these may coalesce in the tubules of the kidney, in the renal pelvis, in the ureter, or in the bladder, with resultant calculus-formation. This is much more likely to occur with sulfapyridine, sulfathiazole, and sulfadiazine than with sulfanilamide. Adequate fluid intake and large doses of alkaline drugs seem to counteract the precipitation of sulfonamide crystals, which occurs much more readily in an acid than an alkaline urine (see p. 1171).

Pathology. Structure and Composition of Renal Stones. A chemical analysis of the stone will help to establish the etiology, and will also indicate whether an alkaline or acid régime is to be recommended, and what elements are to be restricted in the diet. Every calculus, whether spontaneously passed or surgically removed, should therefore be subjected to chemical analysis.

Urinary calculi are of two main types: (1) those formed in an alkaline urine, and (2) those formed in an acid urine. Phosphate and carbonate stones develop in an alkaline urine, while oxalate, uric acid, cystine, and xanthine calculi develop in an acid urine.

Every calculus has a nucleus, which may be a foreign body or urinary crystal. The stone formed about this nucleus may be of simple crystalline structure or laminated, and is presumably held together by a framework, the chemical nature of which is unknown.

A calculus may be pure urate, oxalate, phosphate, carbonate, or cystine, or it may be a mixture of urates and oxalates, or of phosphates and carbonates. Furthermore, a stone which is predominantly phosphate or carbonate may also contain oxalate or uric acid. Joly calls attention to the fact that so-called "pure" stones are rare, and that it is sufficient to consider any calculus which contains from 90 to 95 per cent of any one salt as a pure stone.

The majority of renal calculi are either predominantly oxalates or phosphates. Uric acid and urates, however, appear to be the dominant nucleus. Of 545 calculi examined by Ultzmann, 80.9 per cent had nuclei formed of uric acid. Though uric acid appears to serve very frequently as a nucleus, it forms but a small percentage of the entire substance of the more commonly found types of renal stones. Calcium oxalate is the dominant constituent of renal calculi in America. The constituent next in frequency is phosphate, combined with ammonium, calcium, or mag-

nesium. Exceptionally, stones are found of which the main constituents are pure urate, cystine, calcium carbonate, and xanthine.

Calcium oxalate stones are very hard, usually brown or sepia (though they may be dark gray) and, as a rule, irregular and rough. When small, they are often of a light brown color, with a rough surface covered with sharp crystals or, less often, with spines or spicules. The crystalline stones are of a lighter brown than the spinous ones. The irregular "mulberry calculi" have short, nipple-like projections on all sides save that which has been in direct contact with the pelvic wall; they are frequently of a deep reddish-brown color when not encrusted with phosphates. Because of their roughness and irregularity, calcium oxalate stones tend to be retained until they require surgical removal. Small, oval or spherical stones, sometimes faceted, with a smooth, highly polished surface are also seen. The cause of calcium oxalate is not known, but it is believed that such calculi may result from an oxaluria due to inspissated urine or to increased ingestion of oxalates.

Phosphatic calculi are composed chiefly of calcium phosphate and ammonio-magnesium phosphate in varying proportions, with, as a rule, some calcium oxalate, calcium carbonate, or other salt. The initial nucleus is uric acid or oxalate. The hard, white stones are those made up of crystalline calcium phosphate. One does not often see these, for the majority of phosphatic calculi are of the amorphous type, of mixed composition, and are relatively soft, of a grayish color, and have a rough, granulated surface (e.g., "staghorn" calculus). Stones containing large amounts of phosphates are encountered in hyperparathyroidism and other conditions associated with an increased urinary excretion of calcium and phosphorus. Phosphatic stones are also found in urinary infections due to urea-splitting organisms (*i e.*, *Bacillus proteus*), producing a persistently alkaline urine, and in individuals whose diet contains an overabundance of calcium phosphate.

Uric acid and *urate* stones are hard, ellipsoid or spherical, smooth-surfaced, highly polished, and usually of a golden-yellow color. Both crystalline and laminated types occur. These stones, once mentioned so frequently in any discussion of renal calculosis, are actually seldom encountered. Pure uric acid concretions are practically never removed at operation. Being small, rounded, and smooth, they are usually passed spontaneously, so that the surgeon seldom encounters them *in situ*. *Uric acid*, however, very often forms the nucleus of oxalate or phosphate stones. The etiology of uric acid stones is not clear. They

are commonly, but by no means always, associated with gout, in which there is an increased uric acid excretion.

Cystine calculi are usually crystalline, and are then smooth of surface, polished, and of a greenish or yellowish-brown color. When mixed with phosphates, they are rough and granulated. These stones frequently form typical staghorn calculi. Cystinuria is a rather infrequent disease of unknown etiology. It is believed to be a disorder of the general metabolism. It appears more frequently in Jews than in any other race. Heredity seems to be an important factor. Cystine stones usually occur in children, are generally bilateral, and tend to recur after removal. The reader is referred to the excellent work of Dr. G. F. Cahill and his collaborators, who have reported the results of their extensive investigations upon this subject in the *Journal of Biological Chemistry* (1935-1937).

Xanthine calculi are very rarely encountered in the urinary tract, as is shown by the few reports in literature (16 up to 1937, Kretschmer). Most of them have been found in the bladder. They occur more frequently in young subjects, and oftener in males than in females. Contrary to the statements of most authors, Kretschmer, in a study of the published reports, found that single stones occur more frequently than multiple ones. About two-thirds are composed of pure xanthine, the remainder being mixed. Xanthine stones are usually of a reddish-brown color, compact, rather hard, with an amorphous laminated appearance. With rubbing, they acquire a polished waxy luster. The reiterated statement that xanthine stones are usually negative to the x-ray was not borne out in Kretschmer's case nor in several other reported cases, in which the x-ray examination was positive for stone. Xanthine stones, like cystine calculi, can be explained in no other way than by an error in metabolism.

Soft, non-crystalloid urinary stones are very rare (22 up to 1928, Hyman). They are usually found in the kidneys. Depending upon the predominant constituent, they have been classified as albumin, fibrin, bacterial, and amyloid concretions. Albumin and fibrin stones vary in size from a pinhead to a cherry, are of a wax-like consistency, and are grayish-white, yellow, or light brown in color. Cross sections of albuminous stones show a characteristic lamellation or stratification, and occasionally a nucleus of uric acid or oxalate or blood (Hyman). Bacterial concretions are usually small and multiple. Soft stones are always associated with an infected urine. Pyonephrosis is a frequent complica-

tion. Soft concretions are rarely diagnosed before operation since they cast no shadow.

Foreign-body stones in the kidney pelvis and ureter are also exceedingly uncommon. Exceptionally, calculi are found which have formed around foreign bodies left in the kidney by the surgeon or been inserted into the kidney by traumatic accident.

Location of Stones: Rate of Growth. The great majority of renal stones are found in the lower calyx or the pelvis. This predilection for the inferior calyx has been explained on the ground that, anatomically, this calyx is well below the level of the upper portion of the ureter. As the urinary excretion for each calyx is estimated to be about 3 drops of urine per minute, it is obvious that the urinary stream is far too sluggish to wash crystals and other particles out of a dependent calyx. Marked narrowing or stricturing of the infundibular portion of a calyx also will act to make the calyx retentive.

Joly divides renal calculi into five clinical groups:

- (1) Small stones (usually calcium oxalate) which are still free in a calyx or the renal pelvis.
- (2) Stones impacted at the ureteropelvic junction.
- (3) Stones impacted within the renal pelvis.
- (4) Stones which have become practically a mould of the renal pelvis and calyces.
- (5) "Giant" calculi which have destroyed most of the renal parenchyma.

The stone usually forms in a calyx or the renal pelvis. Here it may be adherent to the wall or lie free in the lumen, gradually increasing in size until it sometimes fills the calyx or pelvis. Frequently, a stone which has formed in a calyx (particularly the upper or middle calyx) is forced out into the renal pelvis, where it may lie free for some time longer, or be washed out toward the ureteropelvic junction. A small, smooth stone will negotiate this junction without difficulty, but a rough, jagged concretion is likely to become impacted at this point. Stones impacted at the ureteropelvic junction soon become moulded into a more or less triangular form. These stones tend to grow backward into the kidney, the growth on the renal aspect of the stone being more rapid than that on its ureteral side. Unless its outlet is blocked, the renal pelvis adapts itself to the presence of a stone in its lumen; urine drains more or less freely around the stone until, eventually, it becomes practically a mould of the pelvis and calyces (the so-called "staghorn" calculus). Sometimes

the stone is of a size actually greater than the normal size of the pelvis in which it has formed, having gradually-distended the pelvic walls as it enlarged.



FIG. 329. Collection of small calculi in the cortex of the kidney. Sectional view of operative specimen.

The rate of growth of a renal stone depends largely on the rate of elimination of the stone-forming salts. In comparison with stones composed predominantly of phosphates, which grow rapidly, calcium oxalate

calculi grow rather slowly. Patients with the latter practically always present themselves for treatment before the stone has filled the entire pelvis and calyces. The large staghorn calculi, moulded to the shape of the renal pelvis, are usually rapidly-forming amorphous phosphatic stones of mixed composition, though the relatively rare cystine stones also often form typical staghorn calculi. Cystine and uric acid stones grow more rapidly than calcium oxalate stones, but not so fast as the phosphatic variety.

Stones do not grow to large size when obstruction is present because, with obstruction, there is impairment of renal function and dilution of the urine, resulting in a decrease of the material necessary for the growth of the stone. On the other hand, renal calculi which do not cause obstruction may reach an incredible size, often giving rise to symptoms so slight that they remain undiagnosed for years ("silent" stones).

Pathological Changes in the Kidney. A kidney which harbors a calculus always suffers from such an experience. A renal stone, however small, is a potential hazard to its possessor, and can never be regarded as harmless. Although staghorn calculi, as well as other single or multiple stones, have occasionally been observed to remain in a kidney for years, apparently giving rise to no untoward results, as a rule infection, with or without obstruction, soon sets in, and an infected calculus is one of the most destructive lesions affecting the kidney.

Stones cause damage to the renal pelvis and parenchyma by obstruction, local irritation, compression of growth, and by infection, which may either precede the stone or result from its presence. The pathological effects upon the kidney will vary considerably, according to the conditions which gave rise to the stone-formation, as well as the size, type, and location of the concretion. A small, pea-sized calculus that has become wedged in the pelvic outlet will cause greater general, as well as local, disturbance than a larger stone which does not obstruct, or only partially obstructs, the free outflow of urine from the kidney.

In the pelvis, the chief effects are those resulting from irritation and obstruction. The presence of the foreign body will cause inflammation of the epithelial lining of the pelvis and calyces; while more or less constant obstruction to drainage from the kidney will result in dilatation and consequent back pressure, constituting a calculous hydronephrosis. Such a hydronephrosis is not, as a rule, of large size, the dilatation being intrarenal rather than pelvic. A stone which completely blocks the outflow of urine from the kidney demands prompt cystoscopic or surgical

removal. If, however, the stone is so located as to cause no interference, or only partial or intermittent interference, with drainage, it may remain undiscovered until infection occurs and greatly complicates the problem.

The presence of infection naturally alters the pathological picture. Destruction of the renal tissue then proceeds with far greater rapidity, stones frequently become multiple, and stone-formation may occur in the opposite kidney. The pathological changes in infections complicating stone are similar to those of non-calculous infections. In the absence of obstruction and hydronephrosis, there will be a calculous pyelonephritis; but when obstruction exists in the presence of infection, a calculous pyonephrosis will be induced, the outlook for which is much graver so far as the integrity of the kidney is concerned. If the infecting organism is of the urea-splitting type (e.g., *Bacillus proteus* and certain cocci), so that the urine is markedly alkaline, the stone soon becomes covered with a phosphatic deposit and may thereafter rapidly increase in size. "A mild staphylococcal infection without distension of the renal pelvis is the most favorable condition for the production of a large branching calculus." The lining mucous membrane, constantly irritated by the presence of the growing stone, tends to shed epithelial cells and to become thick and of a spongy consistency. Suppuration, followed by ulcer-formation, is the next stage, and small hemorrhages in the wounded epithelium give rise to the red blood cells which can be detected in the urine along with the epithelial debris. In general, the condition is one of subacute infection combined with chronic interstitial nephritis. As the stone increases in size, it compresses and thins out the renal parenchyma until frequently there is left but a thin shell of cortical substance. A stone in a calyx may cause blockage of the calyx, which often will be found filled with purulent urine or, in advanced infections, with pus. Such partial pyonephrosis is frequently seen in the presence of a large stone. The secreting tissue of the affected portion of the kidney will be reduced almost to the vanishing point, leaving merely a soft, cyst-like mass, through the yielding walls of which the surgeon can readily feel the contained stone or stones.

Calculous pyonephrosis affecting the entire kidney eventually reduces the organ to a condition resembling a multilocular cyst, often of great size, the dilated calyces forming cavities more or less filled with mucous, debris, and multiple stones. Septa, once the walls of calyces, separate these pockets, all of which open into the renal pelvis. Such a kidney may contain but a single stone, but usually there are several small-sized

calculi, and occasionally large numbers of small stones have been found. In the presence of obstruction, when the kidney inevitably becomes dilated, functional ability is at once lowered and eventually is abolished.

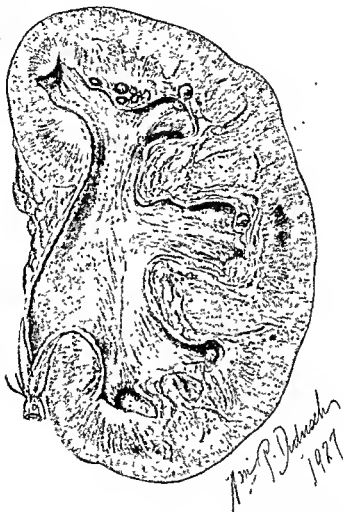


FIG. 330. Multiple small calculi in the renal calyces. Operative specimen.

When the latter occurs, the stone or stones, being deprived of regular deposits of urinary salts, cease to increase in size. This is why the surgeon often uncovers a huge pus-filled sac which was once a kidney, but finds in it only a few stones, or even a single stone, of insignificant size. When such a pyonephrotic kidney is surgically exposed, it will be seen

to have conserved its normal outline, though its external surface will be irregular and knobby. When sectioned, only the merest trace of renal tissue can be found, most often at one or the other of the poles.

Symptoms. Symptoms relative to renal calculi are caused by obstruction, local irritation, and associated infection. As already noted, calculi in the kidney, which do not cause obstruction, may attain great size and result in irreparable damage to the kidney before they are discovered. With improvement in our diagnostic technic, the discovery of these symptomless intruders at a stage when there is still a chance of saving the kidney is becoming constantly more frequent. On the other hand, a small stone which causes blockage of a calyx or complete obstruction at the ureteropelvic junction will cause symptoms of such severity as to compel the patient to seek medical aid at once. The result is prompt cystoscopic or surgical removal of the stone, often before it has had time to seriously damage the renal pelvis or parenchyma. In a sense, therefore, early obstruction by a stone which cannot be passed spontaneously is fortunate, since its removal may thereby be promptly accomplished and the function of the kidney conserved. If the stone is retained, infection inevitably sets in and ultimately results in complete destruction of the kidney.

The most constant complaints are of pain, hematuria, and pyuria.

A majority of the patients give a history of pain on the affected side. This may vary from an occasional twinge or dull ache to the excruciating form of pain known as renal colic. The severity of the pain depends on the degree of urinary obstruction present. A calyx obstructed by a calculus plugging its infundibular portion will give rise to a dull pain in the loin but seldom to a sharp colic.

If a calculus lodges at the ureteropelvic junction, completely obstructing the renal pelvis, a renal colic will ensue which will not be relieved until the stone becomes dislodged. The pain will usually be located by the patient in the loin. It may be referred to a point just over the crest of the ilium and back to the costovertebral angle on the affected side. There is frequently pain and tenderness along the course of the ureter. Hematuria usually accompanies an attack of renal colic. There is rarely sufficient blood to cause clotting. It more often is diffusely mixed with the urine, giving the latter a smoky or a distinctly mahogany color. The total output of urine will be greatly decreased, and occasionally the stone may be so lodged as to induce complete anuria. Anuria also may follow any manipulation of a kidney containing a calculus. It is a most serious

manifestation and one that will tax the urologist's ingenuity to the utmost. Again, anuria may be due merely to the intense pain, in which event relief of the pain will usually be followed by a copious emptying of both renal pelves, constituting a true polyuria. The attacks of renal colic may last only a few minutes, but as a rule they persist for several hours and sometimes for days. Their duration is regulated by the size and surface consistency of the stone, as well as by the progress—or lack of progress—made by the stone in descending the urinary tract. If the calculus does not completely obstruct the outflow of urine, there will be less continued pain than when dilatation is added to the disturbance caused by the presence of the stone itself.

Between the acute attacks of pain there may be showers of crystals or "sand" in the urine. Albumin, blood, and pus are also frequently present in the urine. Unfortunately, the blood is often microscopic in amount and not directly visible. Pyuria is usually present when a stone is large and has inhabited the kidney for a long period.

Diagnosis. The usual preliminary steps of examination—history, general physical examination, kidney palpation, examination of the urine, tests of renal function—will give presumptive evidence for or against renal stone. A history of dull but persistent pain in the kidney area, which increases upon exertion, or of attacks of renal colic, with hematuria or pyuria or both, and the finding of pus, blood, and crystals in the urine, are strongly suggestive of stone in the upper tract. Since these symptoms and signs are not typical of renal calculus alone, but occur in numerous other renal and ureteral conditions, diagnosis based upon symptoms and the findings of urinalysis can only be tentative.

Not only must other conditions in the kidney be ruled out, but the pain must be differentiated from that due to disease of the gall-bladder or appendix, or caused by intestinal obstruction. Many patients with *proved calculous disease of the right kidney or ureter have had a previous history of operation for the removal of the gall-bladder or appendix because of pain in the middle or lower anterior quadrant of the abdomen.*

The main reliance in renal stone must be placed upon roentgenography. A plain x-ray examination, at least, should be made in every case where the clinical history suggests the possibility of stone in the upper urinary tract, or where pus, blood, and crystals are found in the urine. This examination should include the kidneys, ureters, and bladder (Roentgenography of the Genito-Urinary Tract, p. 126). In the properly prepared patient, renal stones can be demonstrated by plain x-ray in a very

high percentage of cases (98 per cent, Joly) because calcium oxalate and calcium phosphate, the predominant constituents of renal stones, cast very good shadows. "Pure" urates and uric acid stones, which cast no shadows, are the exception in the upper tract. Such stones in the kidney or ureter soon become mixed with calcium salts, after which they can be identified by the x-ray. The following findings of the English urologist, Winsbury-White, regarding the relative opacity of urinary stones are of especial interest:

The relative opacity of calculi of equal depth depends upon the atomic or molecular weights of their constituents.

The opacity of a calculus is determined by (1) the nature of its constituents, (2) its structure, (3) its thickness.

Calcium oxalate and calcium phosphate give very good shadows. They are very common constituents of urinary calculi. The high relative opacity is due to the high atomic weight of the calcium present in these salts.

All the other common urinary salts give relatively poor shadows. They include the urates, uric acid, and triple phosphate.

Cystine and xanthine also give poor shadows in the pure state, but of slightly more opacity than the foregoing owing to the sulphur they contain.

It is rare for any of the foregoing substances to be the sole constituents of a stone. This applies to cystine as well as to the more common varieties. There is frequently calcium oxalate or phosphate present.

The plain roentgenogram may show (1) a shadow or shadows indicative of stone, (2) complete absence of shadows, (3) a shadow of doubtful nature. Whether the x-ray be positive, negative, or doubtful, further study—preferably by means of cystoscopy and retrograde pyelography—will be required. Shadows in plain films should be regarded as presumptive evidence only until they are proved by confirmatory urograms and tests. The absence of a shadow in a plain film cannot be accepted as proof that a calculus is not present in the kidney. If stone is present, a filling defect or other abnormality may frequently be observed in a contrast urogram, and should leave a much narrower margin of error. Comparison of the pyelogram with the plain film will help to differentiate renal from extrarenal shadows in doubtful cases.

The plain roentgenogram will show whether the stones are unilateral or bilateral, and give information as to their location, size, and shape, and some idea regarding their number, though this last is not always reliable. The complications of obstruction-infection, which are problems in most of these cases, cannot, however, be studied by this means. Cystoscopy and retrograde pyelography will be necessary (1) to ascertain

how far the presence of the stone has injured the function of the organ, (2) to determine whether or not hydronephrosis is present, and (3) to secure a specimen of urine from each kidney to be examined for the presence or absence of infection and for determinations of the pH and of the type of crystals and sediment present. These are all very necessary procedures for positive diagnosis and the collecting of data which will determine the method of treatment. The pyclogram will also show whether the calculus has formed in a horseshoe, hypoplastic, ectopic, or other congenitally anomalous kidney.

Higgins (1936) has emphasized the importance of determining the pH of the urine from the kidney harboring the stone, due to the fact that in many cases the pH of the urine from the affected kidney is not the same as the pH of the urine from the opposite kidney or from the bladder, even though there is no coexisting infection. In 17 patients in his series it was found that a unilateral urea-splitting organism was present, which would account for the difference in the pH of the urine from the kidney containing the stone. In 11 cases, however, no infection was present in either kidney, but there was marked impairment of renal function and stasis in the kidney harboring the calculus. Since it is essential to determine whether the stone is forming in the presence of an acid or an alkaline urine, it is necessary that specimens be obtained from the kidney which contains the stone.

It is important that the roentgenographic examination be extended to both sides since frequently stones are present in both kidneys but only those in one organ will give indication of their presence.

As a rule, intravenous urography is less satisfactory than the retrograde method for the study of renal stone and the coexisting pathology. While entirely satisfactory in some cases, in others the intravenous urogram leaves a doubt as to the presence or absence of stone. If the renal function is good, the contrast medium will be excreted too rapidly; if poor, no solution may be excreted on that side, and the presence of stone can only be inferred. Therefore, a bilateral ascending pyclogram should be obtained whenever possible. If obstruction prevents this, or if cystoscopy is for any reason contraindicated, a plain x-ray followed by an excretory urogram should be made.

Prognosis. Untreated unilateral calculus may entirely destroy a kidney and yet give no sign. Much more often, however, the untreated stone causes more or less continuous suffering and ill health and eventu-

ally brings about a situation in the urinary tract which is incompatible with life.

With modern methods of surgery, operative removal of the stone, with conservation of the kidney, is possible in many cases. Only too often, however, an irreparably damaged kidney, multiplicity of stones, very large stones, or obstruction-infection makes nephrectomy necessary.

Recurrence of stone-formation following removal is very frequent (Problem of Recurrence, p. 1609). In recent years the incidence of recurrence has been materially lessened in various clinics by postoperative dietary and other therapy. A better understanding of the etiology of stone-formation, improved diagnosis and earlier institution of treatment, and intelligent follow-up observation and treatment of patients who have passed or had surgical removal of a urinary stone have considerably improved, and should still further improve, the prognosis in renal stone.

Treatment. Two problems are involved in the treatment of renal stone: (1) the removal of an existing stone, and (2) the prevention of recurrence of stone-formation following the removal or passage of a stone.

The so-called dietary management of stone is indicated chiefly in the prevention of recurrence. Under exceptional circumstances it may be advisable to substitute this method of treatment for surgery—for instance, in certain cases of small, non-obstructing calculus located in a calyx, or in individuals who have repeated attacks of renal colic and pass small calculi or gravel but show no roentgenographic evidence of stone, or in patients immobilized in bed for long periods because of fractures (these often form renal stones). This plan of treatment is described in a separate section (Problem of Recurrence, p. 1609).

Every stone in a kidney constitutes a hazard to its host; therefore, if it cannot be spontaneously expelled, its removal by operation is usually indicated, though this is seldom an emergency procedure. Caulk states: "A stone in the kidney is actively or potentially a menace—actively if accompanied with infection—potentially if not." Untreated renal stones may cause trouble by destruction of kidney tissue through pressure necrosis, by plugging the ureter at the ureteropelvic junction or obstructing a calyx, by setting up infection or prolonging a preexisting infection in the kidney, or by acting as a focus for the production of infection in the opposite kidney. Even small stones—particularly small, jagged stones in the lower calyx—are a potential source of serious trouble and should not be allowed to go unattended.

The choice of treatment often presents problems which tax the ingenuity and skill of the urological surgeon to the utmost. The number, size, shape, and location of the stones, the presence or absence of infection, the amount of anatomical damage and of functional impairment that the kidney has sustained, and the condition of its mate—these are the chief factors which influence the treatment to be pursued.

Unilateral Stone. Stones located in a calyx, which are too small to block the ureter, may usually be treated expectantly unless a severe infection is present. If smooth and rounded, and particularly if occurring in the upper and middle calyces, these will frequently pass spontaneously. Stones in the lower calyx, particularly if irregular in type, usually call for some form of intervention, though sometimes these too may pass. The usual method, in cases treated expectantly, is to encourage the patient to drink large quantities of water to promote diuresis, give him medication by mouth to keep the urine acid or alkaline, as desired, and keep him on a proper dietary régime to prevent growth of the stone or the formation of other stones, if possible. Dilatation of the ureter, by eliminating obstruction, will sometimes cause small calculi to pass from the kidney. Renal pelvic lavage is useful in causing expulsion of collections of pus and even gravel. We prefer rivanol dextrose, 1:2,000 or acriflavine, 1:2,000. Irrigating the renal pelvis with phosphoric acid, 1 per cent sometimes helps to dislodge calculi, which then will pass through the enlarged ureter. If the stone shows a tendency to descend, it can be watched by x-rays, and it may safely be temporized with for a period of several months, provided no contraindication develops. If, however, marked infection or signs of obstruction are present or develop, prompt operation is advisable, even though stones have been known to exist for years without change. Every patient harboring a stone should have impressed upon him the importance of remaining under regular observation.

Patients with multiple stones present a difficult problem since the chances of complete removal at operation are less than with single stones and the likelihood of so-called "recurrence" is consequently increased. Repeated attacks of renal colic, symptoms of infection or of diminishing function, or roentgenographic evidence of increase in the size or number of the stones call for surgical intervention.

Medium-sized and large stones that are causing symptoms should be removed by appropriate operation whenever possible, since, if they are

permitted to remain, serious damage to the kidney is almost certain to ensue, making nephrectomy inevitable.

If an operation has been decided on, the next question is whether a conservative procedure (nephrotomy, pyelotomy, heminephrectomy, calyceal resection) will serve, or whether a nephrectomy is needed. One cannot be guided entirely by the preliminary urinary, functional, and roentgenographic findings. The condition of the kidney, as revealed at operation, is often of much greater value in arriving at a decision than these preliminary tests. Even severely damaged kidneys often recover to a surprising degree once they have been freed of stones and adequately drained. A kidney with lowered function, but with no evidence of marked sepsis or hydronephrosis, should therefore be treated conservatively.

Removal of the stone should be accompanied by a minimum of trauma. Formerly it was our practice to perform *pyelotomy* whenever that procedure could possibly be done, because it was less destructive than the old method of *nephrotomy* which required closure by mattress sutures, sometimes causing destruction of as much as 25 per cent of the renal substance. Since the introduction of the Lowsley method of repairing nephrotomy wounds by the use of ribbon gut (using pads of fat for hemostasis), nephrolithotomy has become the operation of choice in most of our cases. We now do pyelolithotomy only when the renal pelvis is very large and there is no danger of a stricture forming at the pelvic outlet—a calamity which formerly happened frequently.

Nephrectomy is required when the kidney is so extensively and irreparably damaged that it is useless as a functioning organ.

Heminephrectomy is indicated when the stone and accompanying infection are confined to one pole of the kidney. This operation should be done more often than it now is by most operators.

Resection of a calyx is advisable in certain cases, in order to prevent recurrence. Dependent calyces, and those constricted in the infundibular portion, predispose to the formation of renal stones. In many cases, removal of a stone from such a calyx is followed in a short time by formation of a second stone.

The above operations are described under *Operative Treatment of the Kidney* (pp. 1671, 1672, 1679, 1683, and 1684).

The most urgent indication for immediate operative removal of stone in the upper tract is the occurrence of anuria or marked oliguria due to sudden blocking of the pelvic outlet by a stone—a relatively infrequent but extremely serious complication. In calculous anuria, reflex inhibi-

tion of an opposite kidney frequently coexists. With blockage of the ureter by the stone, the pressure of urine behind it rises and the kidney ceases to function; simultaneously the opposite kidney is reflexly affected and renal activity ceases. Unless the anuria is promptly relieved, death is inevitable. If the obstruction cannot be overcome at once by catheter, immediate operation must be done to remove the obstruction and establish drainage from the kidney. Operation on the reflexly inhibited mate is seldom required.

Stone in Solitary Kidney. Obstruction-producing stone in a solitary kidney presents a very serious and difficult problem. Surgery is usually imperative and, obviously, must be as conservative as possible. As a rule, preliminary catheter or nephrostomy drainage is advisable.

Bilateral Stones. Bilateral calculi always present a serious problem because of the accompanying diminution of function on both sides. Conservative surgery is, of course, an important requisite under these circumstances. Intervention on both sides at one operation is rarely advisable except when rapid bilateral nephrostomy becomes necessary, as it not infrequently does when there are large, infected staghorn calculi in both kidneys or when stones are obstructing both pelves. Generally speaking, when operation on both kidneys is indicated, it is preferable to remove the stones from the kidney showing the better function and less anatomical damage first. This insures good function of one kidney. When the patient has recovered from this procedure, the other kidney is operated upon. Should exposure of the poorer kidney reveal conditions requiring nephrectomy, the surgeon may remove it in the comforting knowledge that its mate is repaired and functioning well. However, if some emergency condition exists in the more seriously impaired kidney, this kidney should be the first one operated on.

Because of the great variation in the clinical picture presented in cases of bilateral nephrolithiasis, it is difficult to establish even general rules as to treatment. Obviously, nephrectomy should be resorted to only under exceptional circumstances, such as when one kidney is pyonephrotic and functionless and absorption from it is causing a strain on the opposite organ.

Follow-up Treatment: Problem of Recurrence. The recurrent formation of urinary calculus following removal constitutes an outstanding problem in urological surgery. The importance of intelligent follow-up observation and treatment for cases of urinary stone cannot be overemphasized. The formation of calculi must be considered a manifesta-

tion of some underlying disease, and surgical removal of a stone is but one phase of treatment. Careful investigation must be carried out to determine the etiological factors responsible in the individual case, and the correction of these factors must be accomplished in order to minimize the formation of recurrent stones. Patients should be examined as frequently as their conditions warrant by roentgenography and urography, supplemented by repeated studies of blood and urinary chemistry.

True Recurrence and Pseudo-Recurrence. True recurrence is the formation of a calculus after complete removal of the primary stone. Pseudo-recurrences are stones or fragments of calculi left behind at operation. Since these fragments may act as nuclei for the further formation of calculi, every precaution should be taken to avoid overlooking them during the operation. Preventive treatment therefore begins at the operating-table. The more general employment of operating-room roentgenography has greatly decreased the danger of leaving stones behind. This procedure is particularly valuable in cases where there are numerous small stones or large branched calculi, and, by revealing stones or fragments left behind, has undoubtedly saved many patients from future operations.

The making of an x-ray postoperatively, before the patient leaves the hospital, should be a routine procedure in cases of urinary stone. If, despite every care, a stone has been overlooked, its presence will at least be known. Unless such a postoperative x-ray is made, it is impossible to state definitely whether a recurrence is true or false.

Soft stones, in the opinion of Higgins, are more likely to recur than those of harder consistency. This is probably because soft stones are likely to leave fragments or "sand" which serve as nuclei for further stone-formation. These particles are difficult to detect during operation, even by x-ray.

Etiological factors that must be considered in the true recurrence of stone are: stasis, infection (local and focal), vitamin-A deficiency, metabolic dyscrasia, and hyperparathyroidism.

Prevention of Recurrence. **STASIS.** The elimination of stasis is an important step in the prevention of recurrence. Though stasis of itself does not cause calculus-formation, when infection is superimposed, retention becomes an important predisposing cause.

INFECTION (LOCAL AND FOCAL). Local infection persisting after the removal of a stone appears to play a predominant role in recurrence. Most investigators are agreed that staphylococci and the *Bacillus proteus*

are of major importance in the re-formation of phosphatic stones. Our own clinical findings agree with this. Schneider and Coudouens, in an examination of 51 cases, concluded that the colon bacillus results in the formation of oxalic calculi and that cocci give rise to uratic calculi. Illyes believes that the formation of calcium phosphate stones may be due to cocci and that a colon bacillus infection may arise later and crowd out the cocci.

Before treatment of infection in the urinary tract can be intelligently planned, it is essential to determine the exact type of offending bacteria. Cocci and the *Bacillus proteus* must be eliminated from the urinary tract if recurrence is to be prevented. Sulfanilamide has been of decided value in eradicating proteus infection, which is extremely resistant to other forms of treatment, such as the high acid ash diet, the ketogenic diet, and the oral administration of acidifying agents. In other types of infection, the sulfonamides, mandelic acid, and methenamine are very useful in eliminating the infection (Urinary Antiseptics, p. 1162). In many instances, particularly in infections with organisms of the colon group, the use of the high acid ash diet and an acidifying agent is sufficient to eradicate the infection, as the pH of the urine is maintained between 5.0 and 5.2 indefinitely.

Pelvic lavage with antiseptics, such as rivanol dextrose, 1:2,000 or acriflavine, 1:2,000, should be carried out. Phosphoric acid, 1 per cent is useful in the treatment of proteus infection.

In most cases, fluids should be forced. The greater the volume of urine, the less likelihood there will be of precipitation of any given crystalloid which may be present in the stone. Also, the forcing of fluids will flush out the urinary tract and help to prevent the collection of pus and debris. In mandelic acid therapy fluids are restricted.

In every patient from whom a stone has been removed, remote foci of infection—e.g., in the teeth, tonsils, sinuses, bowel, prostate, seminal vesicles, or cervix—should be eliminated or at least minimized.

VITAMIN-A DEFICIENCY. In order to assure the presence of ample vitamin A in the diet, it is usually advisable to augment both the high acid ash diet and the high alkaline ash diet with the administration of vitamin A in the form of haliver oil capsules, cod liver oil, or carotene in oil.

REGULATION OF THE pH OF THE URINE BY DIET, MEDICATION, AND FLUIDS. The pH of the urine should be controlled by the use of a diet which is prescribed in accordance with the chemical constituents of the

stone, the object being to regulate the pH to the point at which the salts essential for the formation of a stone are not precipitated. Such precipitation, it has been found, can be prevented by dietary means. However, each patient must be individualized and the closest cooperation between the physician and the patient is necessary.

The stone, when passed or removed, should be subjected to chemical analysis to determine whether the salts present are those which are precipitated in urine with an alkaline or an acid reaction. It is well also to take cultures from the center of the calculus in an effort to determine the presence of bacteria.

(*Acid Diet and Medication.*) If the calculus is found to be composed predominantly of phosphates or carbonates, or if the urine from the kidney which harbored the calculus is alkaline, the high acid ash diet should be prescribed in order to secure acidity of the urine, thereby preventing the precipitation of the phosphates and carbonates of calcium and magnesium, which are the chemical constituents of most recurrent renal calculi (see High Acid Ash Diet, p. 1189). The urine should be reduced to and maintained at an approximate level of from 5.0 to 5.2. It must be tested daily and the acid ash content of the diet regulated according to the pH of the urine until the desired level is reached. If necessary, an acidifying agent, such as ammonium chloride, is given by mouth. Before leaving the hospital the patient should be given instructions regarding the details of the diet and the making of his own daily determinations of the pH of the urine.

As a rule, some supplementary acidifying drug is necessary. The choice of a suitable acidifying agent is of great importance. Most widely used for this purpose has been sodium acid phosphate. However, Barney and Sulkowitch have pointed out that this agent has the disadvantage of increasing the phosphate concentration in the urine. Phosphoric acid is not as powerful as hydrochloric acid and, therefore, phosphatic salts will not increase the acidity of the urine as much as will chloride salts. In their opinion, ammonium chloride should be used by preference because the chloride forms no insoluble salt in normal urine and is to be preferred to ammonium nitrate, which might serve as a second choice, though the use of chloride is more physiological than the use of the nitrate.

Patients on a high acid ash diet do well to drink distilled water or some non-alkaline water, of which Poland water is a good example.

There are certain hazards and contraindications to an acid régime.

With impaired kidney function there is inability on the part of the kidney to excrete acid; in such cases a severe acidosis may result, which will be manifested by a high chloride level and a low carbon-dioxide-combining power of the plasma. Frequent blood examinations are therefore essential during the entire course of such therapy. A similar effect may obtain where kidney function is normal, or nearly so, but there has been restriction of fluids for therapeutic purposes, as in mandelic acid therapy.

Acid therapy is likewise contraindicated when there is present a urinary infection due to urea-splitting organisms, such as the *Bacillus proteus*, which converts urea into ammonia, thus producing an excessively alkaline urine. In this type of infection, the pH of the urine cannot be reduced to the acid side either by the use of the acid ash diet, the ketogenic diet, or acidifying drugs. Acid therapy in such cases is not only useless, but may be definitely harmful inasmuch as this régime leads to an increased amount of calcium and phosphorus in an alkaline urine and hence an increased precipitation of these salts. Oppenheim and Pollak, Barney and Sulkowitch, and others have reported that where such therapy has been utilized, existing stones have occasionally grown larger or more stones have formed.

It must also be taken into consideration that an increased calcium excretion may not be desirable in the presence of calcium oxalate stones. For these patients, a low oxalate diet is preferable (Low Oxalate Diet, p. 1194).

Patients on a Sippy diet for peptic ulcer, who have passed a stone or had one removed, present a difficult problem. The acid régime is helpful in preventing recurrence of phosphatic stones—the type of calculus which usually forms in these cases—but is harmful for the ulcer. An intermediary régime must therefore be worked out for the individual case.

A number of workers have recently pointed out the undoubted fact that an increase in the amount of calcium excreted in the urine is regularly noted when large quantities of acid-producing foods are ingested. The effect of a lower hydrogen-ion content would in this way be offset. Flocks and his co-workers therefore undertook to make quantitative estimates of the relationship. They studied the effect of an acid ash diet and ammonium chloride in two groups of patients: (1) those with excessive urinary calcium excretion, and (2) those having a normal or sub-normal urinary calcium excretion.

When the group with the high urinary calcium excretion was placed upon an acid ash diet, supplemented by 4 grams of ammonium chloride daily, a marked increase in

urinary calcium was obtained. Thus, on an acid ash diet containing 0.8 gram of calcium daily, urinary excretions of 400 to 450 mgm. of calcium daily were obtained.

In contradistinction, the group with the low urinary calcium showed low responses to the same diet and medication. Values of 200 to 250 mgm. of calcium per 24 hours in the urine were obtained. This is of considerable import in the treatment of patients with renal stones by means of the acid ash diet. In the first group, the group showing high urinary calcium, relatively little or no beneficial effect is to be expected from the acid ash diet. Moreover, if urea-splitting organisms are present in the urine, or the slightest amount of stasis is present, harmful effects, such as were obtained by Oppenheimer and Pollack, may result. In contrast, in the second group of patients, those showing a low urinary calcium and a low urinary calcium response to the acid ash diet, this type of diet is ideal, if the desired urinary pH can be obtained.

Flocks calls especial attention to the fact that most preparations containing high vitamin A values are also rich in vitamin D, and that, experimentally, vitamin D has been observed to induce increased calcium excretion in the urine. All his patients, whether from one group or the other, showed an excessive urinary calcium response when placed upon even moderate dosage with vitamin D. The response from patients who already had an abnormally high urinary calcium excretion was much more marked than that obtained from the normal controls. These findings emphasize the necessity of studying each patient individually before attempting dietary treatment.

(*Alkaline Diet and Medication.*) If the stone is found to be composed of uric acid or of cystine, or if the reaction of the urine from the kidney which contained the stone is acid, the high alkaline ash diet with a moderate protein intake of a purine-free nature, supplemented by the oral administration of alkalis, should be prescribed in order to secure alkalinity of the urine and thus prevent precipitation of uric acid and cystine salts (see High Alkaline Ash Diet, p. 1192). The excretion of cystine in the urine is increased by an increase of the protein intake. In general, fluids should be forced as much as possible. It is advisable to use an alkaline water, such as Kalak water.

Frequent examinations of the urine should be made during the process of instituting an acid régime, to ascertain that urates, uric acid, or oxalate crystals are not being precipitated. Likewise, when using an alkaline régime, the urine must be examined for the precipitation of phosphates and carbonates.

RESULTS OF DIETARY THERAPY. That the recurrent formation of calculi can be greatly lessened by proper dietary precautions has been proved. That stones other than cystine calculi can be dissolved by such

therapy is doubtful, although reports of the spontaneous disappearance of stones occasionally appear in the literature.

C. C. Higgins (1936) stated that the incidence of recurrent stone in his clinic was reduced from 16.4 to 4.7 per cent in 4 years by the employment of a dietary régime in conjunction with other, older therapeutic procedures. He also reported a series of 35 individuals with calculi "which have been caused to undergo complete solution and disappearance" following the administration of either a high vitamin A acid ash diet or of a high vitamin A alkaline ash diet, as required. Oppenheimer and Pollak, in 1937, reported the results of their attempts to dissolve calculi by the use of the dietary régime described by Higgins. Twenty-seven patients with single or multiple radio-opaque renal calculi were studied for from 6 to 16 months. "In none was a complete or partial solution of the urinary calculus noted in the frequently controlled x-ray films. Five patients showed an increase in size in their renal calculi, and in one patient a new stone formed while on the régime." In the same year Barney and Sulkowitch reported that patients with phosphate or carbonate stones treated with an acid ash diet and acidifying agents had no recurrence of stone or increase in the size of existing stones. Although in two cases newly formed and loosely formed stones disappeared with the acid treatment, attempts to dissolve well-formed stones were unsuccessful. Both Barney and Sulkowitch and Oppenheimer and Pollak reported an increase in the size of calculi and the formation of new stones in the presence of an infection with a urea-splitting organism as a result of acid therapy.

Although exact statistics are not as yet available, we can unequivocally state that follow-up observation and treatment by means of diet, medication, and the other measures outlined above have materially lessened the incidence of recurrence in our own clinic. The following is an outline of the postoperative régime used by us in our cases of kidney stone during the past 7 years:

A. Examination:

1. Analysis of calculus
2. Serum calcium—serum phosphorus—phosphatase—blood uric acid—urea
3. Differential renal function tests
4. Postoperative x-rays to exclude pseudo-recurrence
5. Bacteriological studies
6. Urinalysis and urinary acidity

B. General measures:

1. General physical examination
2. Elimination of focal infection
3. Maintaining general health at highest level

C. Specific measures:

1. Overcome infection of urinary tract
 - a. Urinary antiseptics: sulfonamides, mandelic acid, methenamine, acriflavine
 - b. Pelvic lavage, ureteral dilatation, indwelling catheters, surgical drainage occasionally
2. Vitamin A
 - Haliver oil capsules, cod liver oil, carotene
3. Alkaline stones
 - a. Acid ash diet
 - b. Keep urinary pH below 5.2; if diet fails to do this, ammonium chloride, dilute nitrohydrochloric acid
 - c. In calcium oxalate calculi, diet low in oxalates
4. Uric acid calculi
 - a. Keep urine markedly alkaline with alkaline ash diet and alkalinizing drugs
 - b. Diet low in purines
5. Cystine calculi
 - a. Intense urinary alkalization
6. Urinary pH determined by patient daily
7. X-ray check every 4 months

Hyperparathyroidism. All patients with urinary stone should be carefully examined for hyperparathyroidism. Particular care must be taken in the examination of the neck to determine whether a palpable parathyroid tumor is present. The calcium and phosphorus content of the blood and the elimination of calcium and phosphorus in the urine should be ascertained. In hyperparathyroidism there is seen a high blood serum calcium and a low blood serum phosphorus, and a high urinary calcium and excessive excretion of phosphate. The finding of osseous changes characteristic of the disease is evidence of great value. Such investigation is of particular importance when renal stones are bilateral or recurrent, and when chemical analysis of the stone indicates its composition to be entirely or largely of calcium phosphate.

In cases of recurrent renal calculi due to hyperparathyroidism, surgical correction of the abnormal conditions in the parathyroids is essential. Whether the renal stone or the tumor should be removed first depends upon the circumstances of the individual case. Upon this point, Church-

ill and Cope (1936), writing upon the surgical treatment of hyperparathyroidism, state:

The tendency at the moment is to regard the disturbance of parathyroid function as a chronic disorder of metabolism which can be handled in due time after the obvious problem of conserving kidney function has been settled. In many instances, as when a calculus is blocking a ureter, this is the correct sequence of procedures. On the other hand, many sequelae of renal surgery such as sepsis and temporary disturbance of renal function may be poorly tolerated or intensified in the face of severe hyperparathyroidism. These same sequelae of renal surgery may in turn make proper handling of the hyperparathyroidism more difficult. The only answer that can be offered at the moment is that the urologist must consider the disease as a whole and not endanger the patient by myopic regional surgery. As a general rule, the initial step in treatment will be the correction of basic disturbances in metabolism. Although the skeletal changes incident to hyperparathyroidism are crippling and painful, the real hazard of the disease is the damage suffered by the kidneys. . . . Only a failure to grasp this fact can account for a revival of the treatment of hyperparathyroidism by dietary measures. . . . The treatment of hyperparathyroidism by a diet high in calcium and phosphorus is not only inadequate but positively dangerous.

These authors consider renal impairment to be one of the main indications for partial resection of the parathyroids.

Dissolution of Calculi by Chemical Means. We have been able to dissolve newly formed phosphatic calculi in a few instances. Most of these were recurrences that had taken place during postoperative convalescence. The citrate solution originally employed by us for irrigating the renal pelvis was composed of sodium citrate, 45.2 Gm., citric acid, 38.0 Gm., and distilled water to make 1,000 cc. This, however, is irritative to renal tissue and is often followed by pain, hematuria, and pyrexia. We have had better results with the following solution ("G" solution):

Citric acid monohydrate	32.875 Gm.
Magnesium oxide anhydrous.	3.840 Gm.
Sodium carbonate anhydrous	4.370 Gm.
Distilled water sufficient to make	1000 cc.

Resulting pH should be 4.0 when solution is ready for use.

Autoclave solution at 15 pounds pressure for 20 minutes.

The pelvis is usually irrigated through a No. 5-F. catheter, and drained through a No. 8 or 9-F. catheter. If a nephrostomy tube is still in place, we employ through-and-through irrigation.

Movable Kidney (Nephroptosis)

Introduction. The normal kidney is loosely fixed by the vascular pedicle, fatty capsule, perirenal fascia, and intra-abdominal pressure,

and moves from 2 to 5 cm. in its niche with respiration. It also moves with change of bodily positions. A comparison of pyelo-ureterograms taken with the patient in the dorsal and erect positions will show that the kidney normally drops as much as 10 to 12 mm. with assumption of the upright posture. The ureter and renal pedicle adjust themselves to these slight changes of position without disturbance of function.

By the term "movable kidney" is usually indicated one whose excursions exceed the normal movements incident to respiration and change of posture. It includes those kidneys discernible by palpation, as well as the rare, congenital "floating" kidney which has become intra-abdominal and may wander even across the median line.

A palpable kidney, however, is not necessarily abnormally mobile or in any way pathological. In a thin person it is always possible, during deep inspiration, to palpate the lower pole of the kidney. Moreover, abnormal movability is not in itself pathological. In many individuals, whose kidneys undoubtedly have a greater range of motion than normal, there are absolutely no symptoms which can be related to this condition. The blood supply and the ureter, in these cases, adjust themselves so readily to the changes of position that there is no functional or symptomatic disturbance, and the abnormal movability is usually discovered during a routine physical examination. Movability becomes pathological when it impedes free urinary drainage, or causes disturbances of the renal blood or nerve supply, producing symptoms referable to the urinary tract, or reflex gastric or nervous symptoms. Clinically, therefore, two groups of movable kidneys must be differentiated: (1) nephroptosis without symptoms or functional disturbances, (2) nephroptosis with symptoms. The first group requires no treatment and is of little clinical importance.

Historical. The earliest reference to the subject of nephroptosis is that of Meuse, of Venice, published in 1495. Rayer discussed it in his epochal classic, produced in 1841. In 1859 Dietl described the condition since known by his name—Dietl's crisis. Hare, in 1860, advocated the use of elastic abdominal belts to support ptosed kidneys. The first suspension was done by Hahn, of Berlin, in 1881. In the later years of the nineteenth century and the opening decade of the twentieth there was a period of over-enthusiasm when all patients in whom movable kidneys could be demonstrated were subjected to nephropexy, and the operation achieved the proportions of a fad. This abuse of nephropexy

was followed by a period of time in which the operation was discredited, and the nephroptotic patient was surgically neglected. During the past twenty years there has been marked advance in the diagnosis of renal disease. The tendency at present is to believe that nephropexy is a very useful operation in properly selected cases of nephroptosis, but that by no means all cases require kidney elevation.

Incidence. Mobility of the kidney has been variously reported in medical literature to be present in from 18 to 22 per cent of all women (18 per cent, Kidd, MacKenzie; 20, Hinman; 22, Glenard, Edebohl, Kelly and Burnam), and in from 1 to 2 per cent of all men (1 per cent, Kidd, MacKenzie; 2, Hinman, Kelly and Burnam). In Mathé's series of 90 cases, there were 72 women and 18 men; in Deming's series of 74 cases, there were 63 women and 11 men. Of 263 patients with symptom-producing nephroptosis seen at the Squier Urological Clinic of the Presbyterian Hospital, New York, from 1928 to 1938, 221 were females and 42 males (Fish and Hazzard). Of 47 patients with nephroptosis seen at the Brady Urological Foundation, of the New York Hospital, during 1937 and 1938, 42 were females and only 5 males.

When the ptosis is unilateral, the right kidney is involved much more frequently in women; but in men the involvement of the right and left sides is more nearly equal. Bilateral involvement is relatively common. Of 38 patients who had nephropexies for primary nephroptosis at the Brady Foundation from 1921 to 1935, 28 had a right nephropexy, 4 a left, and 6 both right and left (Church, 1936). Of the 47 patients seen at the Brady Foundation in the years 1937 and 1938, 43 had right-sided nephroptosis, 4 bilateral ptosis, and in no instance was there ptosis of the left kidney (Hawes, 1938). Fish and Hazzard found ptosis of the right kidney in 166 patients, of the left kidney in 25, and of both organs in 72. Deming found the right kidney involved in 53 cases, the left in 11, and both sides in 10.

Though young girls occasionally suffer from movable kidney, in the vast majority of cases the condition does not manifest itself until after puberty. Many patients are in the third decade of life, but the greatest incidence (40 to 50 per cent) is between the ages of 30 and 40 years. Thereafter, the number of cases declines, although nephroptosis is not uncommon in the elderly and even the very aged.

Etiology. Nephroptosis results from a combination of congenital and acquired factors.

Of congenital factors predisposing to movability of the kidney, certain

peculiarities of bodily form apparently play an important part. In subjects with movable kidney the renal fossae are not only smaller than normal but are widely dilated at their lower ends. The constant finding of these shallow, cylindrical or funnel-shaped fossae in subjects with nephroptosis led Wolkow and Delitzin to conclude that the condition results from an anatomical deficiency of the renal fossae. The tall, slim Iberian type with narrow hips is likely to have a small renal fossa, from which the kidney is prone to descend.

A relaxed perirenal fascia is another factor which predisposes to movability. It will be recalled that the kidney is confined in its fossa by means of fascial coverings (*Anatomy of the Kidney*, p. 1352). The perirenal fascia, which above is attached to the diaphragm, splits into an anterior and a posterior leaf at the lateral border of the kidney, at about the level of the adrenal gland. These two layers form a sheath for the kidney but do not completely surround it. The anterior leaf passes medialward in front of the kidney and behind the peritoneum to join with the corresponding leaf of the opposite side in front of the great abdominal vessels. The posterior leaf extends medialward behind the kidney to find an attachment on the side of the spinal column. Below, the perirenal fascia blends with the subperitoneal fascia. Numerous trabeculae, which traverse the adipose capsule, connect this sheath with the fibrous capsule of the kidney and help to hold the kidney in position.

In quadrupeds, the anterior sheath of the perirenal fascia, which here is thick and strong, alone supports the animal's kidneys and restrains them from dropping down and pressing upon the abdominal viscera. The erect position in man, however, calls for less strain, and here the sheaths are thin and frequently defective. A defect in either the anterior or posterior leaf of the perirenal fascia is of itself sufficient to explain the etiology of a ptosed kidney. In many thin females the fatty capsule is lacking, so that the weight of the kidney is placed upon the trabeculae, causing them to become stretched. This, with relaxation of the perirenal fascia, allows the kidney to move from its fossa.

Attachment of the perirenal fascia lower down than normal in the postperitoneal layer is frequently noted in subjects with nephroptosis, and may be a predisposing factor in some cases.

The more frequent involvement of the right kidney is attributed by Mathé, in part at least, to the fact that the right renal fossa is more shallow than the left and has a wider lower end, with a relatively lower attachment to the hepatic flexure. The explanation of Sir Arthur Keith is that

the right fossa is roofed in by solid liver, communicating directly to the kidney the downward pressure of the diaphragm. Any factor which tends to reduce the size of the sub-diaphragmatic space will compress the liver and force the right kidney downward. The spleen on the left is much smaller than the liver, and the stomach and colon are hollow. Hence the right kidney is far more often subjected to such pressure than is the left.

An important secondary factor in the causation of nephroptosis is loss of muscular tone of the abdominal wall. The kidney is held in position not only by means of its fascial coverings and the perirenal fat, but also by intra-abdominal pressure. The tension within the abdomen is maintained by the tone of the muscle of its wall; hence anything which leads to loss of this muscular tone may result in visceroptosis and nephroptosis. Women whose abdominal-wall muscles have become flabby and lacking in tone, as sometimes happens after repeated pregnancies, are liable to develop nephroptosis. So also are sluggish, non-athletic women of poor posture, as well as slender, poorly nourished women who have never borne children but are lacking in perirenal fat.

Other secondary causes of nephroptosis are various types of trauma. It is often stated that sudden, violent muscular exertion, such as heavy lifting or straining, may cause nephroptosis, but it is our impression that this is rarely so. On the other hand, there is definite reason to believe that long-continued jolting or other forms of vibration, such as one experiences on long train trips or automobile rides over rough roads, may have an influence on descent of the kidney in one predisposed to the condition.

Occupation may be a contributory factor in the production of nephroptosis in one who has a congenital defect in the renal sheath with weakness in the renal supports. Women, especially, who are subjected to long hours of standing or continual bending, may have a predisposition to ptosis greatly exaggerated.

To summarize: It seems to be the consensus of opinion that certain peculiarities of bodily form—namely the shallow, funnel-shaped or cylindrical fossa of Wolkow and Delitzin—together with loss of security of the kidney due to the upright posture, and laxness of the perirenal fascia, predispose to nephroptosis, and that various factors often cited, such as pregnancy, tight lacing, loss of perirenal fat, or trauma, operate only as secondary factors in those predisposed to abnormal renal mobility. The fact that women are much more subject to this condition than men

is probably because the renal fossa in women is wider and shallower in its lower part than is the case with men.

Pathology. An interesting feature of nephroptosis is the lack of evidence of degenerative changes in the renal substance. The vascular pedicle may become markedly elongated, the ureter distorted, and there may be thickening of the renal pelvis and capsule, with adhesions to the perirenal fat, but the kidneys themselves usually show no pathological change unless chronic infection has been present. As a rule, the function is normal or only slightly impaired. Back pressure, due to kinking or stricturing of the ureter, results in hydronephrosis; this, however, is usually of moderate degree.

Symptoms and Signs. Not all ptosed kidneys produce symptoms. Mobility is of first, second, and third degree, and each may be with or without symptoms. The factor governing the production of symptoms is not the degree of ptosis, but the effect of mobility upon the vascular pedicle, ureter, and peritoneal and other attachments. The floating kidney, which often has a long pedicle and a loose, tortuous ureter, frequently causes no symptoms, while a moderately ptotic kidney may show pronounced symptoms.

The ureter of a ptosed kidney is redundant, and must therefore pursue an abnormal course. Even a moderately ptosed kidney may drop sufficiently to kink the ureter over a blood vessel, fibrous band, or its attachment to the perirenal fascia, or so move that a temporary constriction or occlusion of the ureter occurs. It will be recalled that the upper part of the duct lies within the perirenal capsule, but that lower down it passes over the perirenal fascia, being held in place by the overlying peritoneum, so that at this point its position is firmly established. Should the kidney sag below the ureter's point of attachment to the perirenal fascia, kinking is practically certain to occur; but, if the kidney is freely movable, resumption of the recumbent position will tend to straighten out the kink, so that obstruction is *not likely to occur*. However, such a kink can easily become permanent if the kidney fails to return to its normal position. Thus, women predisposed to nephroptosis, whose occupations require standing for long periods, are much more likely to suffer from the results of ureteral blocking than those who are able to change their positions more frequently. It has been repeatedly demonstrated that kinks of the ureter may be present without producing symptoms, and that it is only when the kink becomes *fixed by adhesions or other accidental causes* that there will be stasis and back pressure sufficiently

constant to produce hydronephrosis. The lumen of the ureter may also be occluded by the rotation of the kidney about its vertical axis, a common observation in movable kidney.

Though ptotic kidneys are by no means always infected, such kidneys are undoubtedly more subject to infection than normally situated organs. Sagging kidneys were put forward some years ago by Crabtree and Sheddon as being an important factor in the persistence of colon bacillus pyelitis. Kinking or stricturing of the ureter, by interfering with free urinary drainage and causing stasis, is probably the most potent factor in the persistence of infection. Statistics show that a large percentage of subjects of nephroptosis (from 33 to 70 per cent in various series) have infected urine. This is probably due to the fact that an accidental infection has failed to clear up because drainage by way of the ureter was impeded. Some of the extraurinary symptoms which often accompany nephroptosis, particularly the neurotic phenomena, may be due to toxic absorption secondary to failure in renal drainage. Infection may be present without obstruction and stasis, in which event its relation to movability is always in doubt.

The symptoms of nephroptosis may vary greatly, depending upon whether or not there is obstruction and infection, and upon the effect of ptosis on adjacent organs. The common clinical picture presenting a complex train of symptoms referable to the urinary, gastrointestinal, biliary, and nervous systems should always suggest the possibility of nephroptosis, and these cases are usually readily diagnosed. So, also, are the cases with symptoms referable to the urinary tract. In these two groups there is usually definite kinking or stricturing of the ureter, with more or less hydronephrosis or infection, or both. Much more difficult to diagnose correctly is the type of case presenting symptoms elsewhere than in the urinary tract. It is well known that gastrointestinal and nervous manifestations are frequent accompaniments of nephroptosis, and may be the only symptoms. When these occur with localized pain and symptoms of urinary-tract obstruction or infection, they fit into the clinical picture of nephroptosis; but when they occur without symptoms referable to the urinary tract, they may be extremely difficult to interpret.

Pain. Pain is the most prominent complaint, and may be acute or chronic. It may be merely a feeling of weight or a dragging sensation, or it may occur in the form of a more or less constant dull ache, or in severe, acute attacks (Dietl's crises). The dull ache is usually localized

in the loin or, if the kidney is very low, in the lower abdomen. As a rule, it does not radiate. It is relieved by lying down, and is aggravated by exercise, long periods of standing, constipation, and menstruation. Dull pain is present when there is partial obstruction of the ureter and back pressure.

The Dietl's crisis is the result of kinking of the ureter or torsion of the renal pedicle. It occurs suddenly, with violent abdominal pain, which is often accompanied by nausea, vomiting, and chills, and sometimes by fever and collapse. As the acute attack subsides, there follows a period of dull ache or soreness in the affected side, which may subside entirely or continue between the acute attacks. If the acute attack is due to kinking of the ureter, relief of this will usually be followed by a transient polyuria and disappearance of the acute symptoms; but if the crisis is caused by torsion of the pedicle, inducing an intense venous congestion in the kidney, with increased intracapsular tension, the attack will not subside so quickly. Temporary hematuria may follow such a seizure. Acute attacks are often dated by the patient to a definite incident, such as a strain, blow, or prolonged coughing attack. Frequently, however, they occur without any apparent inciting cause. The Dietl's crisis due to movable kidney must be differentiated from similar acute attacks caused by the passage of a ureteral stone or a blood clot.

Reflex pains to the epigastrium are common, and occasionally there may be referred pain in the rectum, perineum, vagina, or testis.

Gastrointestinal, Nervous, and General Symptoms. The most common extraordinary manifestations are disturbances of the digestive system, such as nausea, vomiting, flatulence, constipation or diarrhea, and, occasionally, jaundice. The position of the cecum and transverse colon usually changes with the excursion of the kidneys, which, in turn, may produce either constipation or diarrhea, though stasis and obstruction to the normal emptying of the bowel are more common than excessive motility. Kinking of the cystic duct, due to displacement of the gall-bladder or duodenum by the downward pull of the peritoneal attachments, may cause jaundice. Associated visceroptosis is fairly common, and when this is present the nephroptosis is usually bilateral. In women, ptosed kidneys may cause such pressure on the pelvic organs as to produce symptoms referable to them. Many patients give a history of a previous appendectomy or operations upon the female adnexa or gall-bladder.

Fatigue is a very common symptom. Patients tire easily, and can often perform their ordinary tasks only with great effort.

Nervous symptoms, such as insomnia, dizziness, hyperesthesia, emotional disturbances, and even hysterical states, are also common. In most cases they are probably the natural result of a long period of chronic pain and discomfort, and correction of the renal abnormality will usually result in disappearance of the nervous and neurasthenic manifestations. The general and hormonal symptoms have been ascribed by Fowler, Bell, Hess and others to stretching of the sympathetic fibers that accompany the renal pedicle and disturbances of circulation in the adrenal gland, which is usually dragged down with the kidney. As a result of circulatory deficiency, "the adrenal will be adversely affected, and these hormonal effects upon the sympathetic nervous system may help to cause the nausea, pain, and the neurotic symptoms which seem to predominate." (Hess)

Urinary Symptoms. Urinary symptoms are seldom present unless there is a coexistent infection. The latter, however, is fairly common, and is usually due to the colon bacillus. Infected patients show symptoms of frequency, urgency, scalding, and burning. Pyuria is frequent; and occasionally there is hematuria, as a result of kinking of the ureter and distention of the renal pelvis. A transient polyuria is sometimes noted after an acute attack.

Diagnosis. Not only must abnormal mobility be established, but it must be determined whether the mobility is responsible for the symptoms and disturbances. A careful history, physical examination, and urological investigation are necessary in order to (1) establish abnormal mobility, (2) determine the presence or absence of hydronephrosis and infection, (3) differentiate associated abnormalities, such as stricture, kink, aberrant vessels, fibrous bands, high insertion of the ureter, and periureteritis, (4) decide whether treatment should be palliative or surgical.

The common clinical picture is pain, obstruction, infection, gastrointestinal disturbances, and nervous symptoms extending over a considerable period of time. Localizing symptoms may, however, be absent, and in these cases proper interpretation of the relation of mobility to the gastrointestinal and nervous symptoms may be very difficult.

Palpation may or may not reveal mobility or tenderness of the affected kidney. Frequently, however, the kidney can be palpated, and in some cases moved about quite freely. The patient should be examined standing and sitting. In the recumbent posture the kidney may return to its

normal position, and if palpation is done in this position alone, its errant tendencies may go unnoticed.

Urological investigation should include examination of the urine, relative function tests, ureteral exploration with bulb and wax bulb, plain roentgenograms, pyelo-ureterograms in the prone and upright positions, and determination of the pelvic and ureteral emptying time. Accurate diagnosis can only be established by correlation of all the findings.

Urinalysis is of little diagnostic value except in dealing with coexistent infection. Albumin is practically always present, probably because the excursions of the kidney impede its circulation, with resultant congestion of the organ. Blood and pus are common findings, particularly the latter.

The function of the ptosed kidney is seldom modified to any considerable extent, and in many cases shows no diminution. Approximately 60 per cent of our cases, however, have shown some decrease on the ptosed side.

Roentgenographic Examination. Although abnormal movability of the kidney can often be established by the usual preliminary examination, pyelo-ureterograms are necessary to determine whether the mobility is the cause of the pain or other symptoms complained of by the patient, and to decide the treatment to be instituted. The degree of mobility and of hydronephrosis, and the presence of distortions of the pelvis and ureter, may be determined in most cases by retrograde pyelography with the patient in the recumbent and erect positions. Excretory urograms are less satisfactory, since the ureter is rarely filled. In making the exposure in the erect posture, the catheter must be withdrawn below the point where the ureter receives the support of its peritoneal and fascial covering. This will permit the unsupported upper end of the ureter to assume the position forced upon it by descent of the kidney; whereas, if the catheter remains in the lumen, it will keep the ureter straight, even when the kidney descends under the influence of gravity. The presence of infection of the renal pelvis may also be ascertained by pyelography.

Injection of the renal pelvis will often cause a duplication of the pain which the patient has suffered—a valuable diagnostic point in some cases.

SERIAL PYELOGRAMS. Serial pyelograms are highly desirable in the study of nephroptosis, particularly when renal pelvic retention is suspected. Single urograms cannot be relied upon for the recognition of ureteral kinks and strictures, fixed pelves or ureters, aberrant vessels,

constricting bands at the ureteropelvic junction, or atony of the ureter. Multiple x-rays are necessary to distinguish between physiological and pathological distortions of the pelvis and ureter, and to determine whether there is interference with emptying of the pelvis and ureter.

In the investigation of pain syndromes referable to the upper urinary tract, serial films are invaluable, and should be made in all cases where it is believed that delayed emptying may be the cause of the pain. In common with many urologists today, we believe that nephropexy is seldom indicated or beneficial in a ptosed kidney unless it can be demonstrated that there is obstruction to renal and ureteral drainage, and that the pain is apparently due to distention of the renal pelvis. It is our impression that renal mobility alone rarely produces pain, and that ureteral kinks in nephroptosis are of no particular clinical importance unless there is evidence of renal stasis or chronic infection of the renal pelvis. The transient nature of ureteral kinks occurring with nephroptosis has often been noted. As pointed out by Thompson and Bumpus in 1930, a common cause of kinks at the ureteropelvic junction is the order to "take a deep breath and hold it" while the film is being exposed; descent of the kidney with the diaphragm results in kinking of the ureter. In the interpretation of ureteral kinks, therefore, the factor of respiration must always be considered.

The amount of mobility, as already noted, is no criterion of the emptying time of the pelvis. The renal pelvis may empty readily although there is marked mobility with resulting tortuosity of the ureter; on the other hand, its drainage may be impeded in some cases showing only slight mobility. Mathé, who has carefully studied the movable kidney in its relation to hydronephrosis, believes that mobility alone does not cause hydronephrosis; but if, during descent of the kidney, the redundant upper portion of its ureter presses on or kinks over an aberrant renal vessel, fibrous band, or the ureter's upper attachment to the perirenal fascia or to the posterior peritoneum, obstruction will occur, resulting in hydronephrosis.

At the Brady Urological Foundation, of the New York Hospital, we have used serial pyelograms for a number of years as an aid in deciding the type of treatment to be instituted, and frequently we have found that kinks of the ureter and apparent stasis of the pelvis and ureter produce no interference with urinary drainage.

The serial pyelographic tray devised by Thomas D. Moore in 1931 provides a simple, inexpensive, and practical method of studying the

emptying time of the renal pelvis and ureter. This is a modification of the Bucky diaphragm tray. Six exposures of a kidney and ureter can be taken on two 14 by 17 inch films, thereby demonstrating the emptying time of the upper urinary tract and, in addition, furnishing a series of films which enables one to distinguish functional from pathological changes. Exposures may be taken in the supine or erect positions.

The taking of serial pyelograms is described elsewhere in these pages, and need not be repeated here (see *Serial Pyelography*, p. 133).

Treatment. Not all patients with nephroptosis require surgery. Many show no symptoms whatsoever, and should therefore be left alone. Others, especially those with kinks, respond to dilatations of the ureter. Some respond to kidney belts, with a suitable hygienic regimen.

Conservative Treatment. Conservative measures should first be tried in all but the most pronounced examples of renal mobility. It is our practice to treat patients conservatively for several months before advising surgery. Such treatment consists of an abdominal support, exercises to improve the bodily posture and strengthen the relaxed muscles, and a dietary and health régime calculated to add weight to the patient in the hope that the perirenal fat will be increased sufficiently to maintain the kidney in its proper location. Rest in bed for from 4 to 6 weeks, with the foot of the bed elevated, together with forced feeding and other measures directed toward improving the systemic condition, is sometimes productive of excellent results, especially in cases with general visceroptosis. Thereafter, a carefully fitted belt should be used.

Opinions differ regarding the efficacy of kidney belts in relieving the symptoms due to a ptosed kidney. It has been our experience that a well fitted and properly applied belt will frequently relieve all symptoms, if used in conjunction with a suitable prophylactic routine, provided there are no coexistent disabilities of the urinary tract. However, permanent relief from the use of the belt cannot be expected when there are associated abnormalities of the ureter or pelvis resulting in interference with drainage and stasis. In such cases surgical fixation is frequently required. Many women prefer a combined girdle and belt. The belt should be tightened from below upward, and should be adjusted with the patient lying down, with the hips elevated.

If infection is present, with obvious stasis, operation is indicated; but in the absence of stasis, the infection should be combated by the usual measures in the way of diet, drugs, and chemotherapy. Moderately infected cases, with slight delay in pelvic and ureteral emptying, some-

times become free from infection after a few dilatations of the ureter and irrigations of the renal pelvis.

Surgical Treatment. Operation should be done on carefully selected cases only. We believe that, as a rule, inadequate drainage must be proved before surgery is indicated. Many physicians and surgeons have been prejudiced against nephropexy by unwise selection of cases. Fixation of the kidney is rarely indicated or beneficial unless there is interference with pelvic and ureteral drainage, with stasis or infection or both; on the other hand, in carefully selected cases, a properly performed nephropexy, together with decapsulation, ureterolysis, ureteropyeloplasty, ligation of aberrant vessels, or sympathectomy, as indicated, is curative in a high percentage of cases. Movability alone is seldom responsible for the production of symptoms, and frequently fixation of the kidney is but part of the surgical treatment.

When conservative measures have failed to relieve the symptoms, or when there is evidence of progressive obstruction and infection under their use, or when, as frequently happens, the patient cannot endure the pressure of a kidney belt, nephropexy should be considered (*Operative Treatment of Nephroptosis*, p. 1699).

Occasionally a case of nephralgia, without evidence of obstruction, will be encountered; for these we recommend denervation and decapsulation.

Nephroptosis associated with visceroptosis is practically always bilateral. Symptoms in these cases are due to the general visceroptosis, and nephropexy will not benefit the condition. In fact, elevation and fixation of both kidneys is likely to add to rather than relieve the patient's discomfort because the liver takes part in such sagging and would press down upon the elevated right kidney. A properly fitted belt will usually relieve the patient of many of the subjective symptoms. These patients, as previously stated, are often greatly benefited by rest in bed for several weeks, with a diet and health régime calculated to increase the weight and improve the general systemic condition.

Renal Diseases in Children

Both congenital and acquired abnormalities of the kidneys are commonly manifest in infancy and childhood.

Congenital Anomalies of the Kidney. Congenital anomalies and malpositions of the kidney have been considered on page 1361, and ureteral

anomalies on page 1213. They are frequent and extremely important factors in the renal diseases of childhood.

Hydronephrosis. Hydronephrotic kidneys are a not uncommon finding in the newborn and in young children. The juvenile phase of the subject has been adequately considered in connection with hydronephrosis in adults.

Non-specific Renal Infections. *Staphylococcic infections of the renal cortex* (staphylococcic suppurative nephritis, cortical abscess, carbuncle) occasionally are encountered in children. As with adults, in such cases there is usually a history of preceding superficial pyogenic infection or infection of the upper respiratory tract. These infections of the kidney, in children, are treated the same as when they occur in adults.

Acute simple pyelonephritis, or pyelitis, as it is generally termed, is common in children. This is usually due to invasion by the colon bacillus. When properly treated by the accepted methods, recovery should take place in from 3 to 6 weeks. When this does not occur, or when there are relapses of such an infection, or the microscopic picture or culture reveals evidence of pus or bacteriuria, search for an accessory factor should be made. *Chronic infections* are usually of the obstructive type, the obstruction being some form of congenital anomaly as a rule. Congenital malformations of the urinary organs are frequent, and in a large proportion of cases they are the principal factor influencing the severity and duration of pyelonephritis in childhood. Bacteriuria, pyuria, and other types of urinary disturbances are often but the clinical manifestations of structural defects in the urinary tract. These are readily delineated in a urogram, and intravenous or retrograde pyelography should be done in every case of persistent or recurrent pyelonephritis in children. Either of these procedures can be done with safety in even very young children.

Except for their greater incidence in female children, the common renal infections of infancy and childhood present no special peculiarities, and are therefore taken up with those of adults.

In children, acute renal infections not infrequently complicate such infections as otitis media, tonsillitis, and sinusitis; or they may occur in the course of an infectious fever.

• **Perinephritic Abscess.** Perinephritic abscess is sometimes encountered in children and even in infants, but perinephritic and cortical renal suppurations are much more frequent sequelae of staphylococcic infection in adults than in children, in whom osteomyelitis is the common sequel.

Specific Infections. Aside from tuberculosis, specific infections of the kidneys in children are decidedly rare. A few cases of hydatid cyst have been reported. Probably children are no more immune to this infection than adults, but the growth of a hydatid cyst is exceedingly slow, and as a rule it takes years for the cyst to attain a sufficient size to cause symptoms.

Actinomycosis of the kidney in children has also been reported, usually in association with actinomycosis elsewhere in the body.

Renal Tuberculosis. *The recognition of renal tuberculosis as a fairly common disease of childhood and adolescence is a recent advance in the management of tuberculous infections. Due to the perfecting of small-caliber child cystoscopes, it is now possible to make a systematic routine urological study of suspected cases in even very young subjects. This, together with the greater interest in urology in children, has resulted in the clinical diagnosis of many cases which, formerly, would have gone undiscovered, or been revealed only at autopsy, or by pathological study of a supposedly pyonephrotic kidney after nephrectomy. Despite this improvement in diagnostic methods, however, renal tuberculosis in the child and in the adolescent is often overlooked.*

Incidence. Campbell, in a study of 312 infants and children with chronic pyuria, found 5 (1.5 per cent) with renal tuberculosis. In 2,420 autopsies in his pediatric service at Bellevue Hospital (New York), 4 cases of "surgical" renal tuberculosis were found. Mathé, reviewing 4,698 cases of unilateral surgical renal tuberculosis, found 71 cases (1.5 per cent) in infants and children aged 1 to 10 years, and 494 cases (10.5 per cent) in adolescents aged 10 to 20 years. Webster, of the Children's Hospital in Melbourne, while providing no exact figures, gives as his opinion that "clinically appreciable tuberculosis of the kidney is uncommon in childhood, but tuberculous infection, inducing minor and symptomless lesions, occurs more frequently than has been realized in the past." Addison, of London, states that miliary tuberculosis of the kidney is a frequent finding in children dying of meningitis or of generalized tuberculosis.

Etiology. Tuberculosis of the kidney in children is always secondary to a focus elsewhere in the body. The initial lesion is most commonly in the lungs, but primary foci in the bones and joints, lymph nodes, and intestinal tract are also frequent. In adolescent male patients, the primary lesion is occasionally in the prostate gland or (rarely) in the seminal vesicles.

Infection usually invades the kidneys by way of the blood stream, but occasionally might be lymphogenous in origin.

Pathology. Prior to 5 years of age, renal tuberculosis is most often of the bilateral medical type, and is frequently part of a generalized miliary tuberculosis. Tubercles are usually scattered throughout the renal substance, and caseation and cavity-formation do not occur. The mortality in this age group is very high, the patient usually dying from dissemination of the disease throughout the body.

Above 5 years, the unilateral surgical type is more likely to be recognized.

Symptoms and Diagnosis. The symptoms of renal tuberculosis are at no time pathognomonic, and this is particularly true in childhood. In the bilateral, miliary type of tuberculosis usually seen in young children, the signs and symptoms are those of nephritis. The urine is clear, and contains tubercle bacilli, albumin of hematogenous origin, hyaline and granular casts, but little, if any, pus.

In the unilateral, surgical type of tuberculosis, the symptoms depend largely upon the extent of vesical involvement. In every case of chronic cystitis, relapsing pyelonephritis, and persistent pyuria in children, renal tuberculosis should be suspected and searched for. What has been said regarding the pathology, symptoms, and diagnosis of chronic renal tuberculosis in adults applies, for the most part, to children and adolescents as well, so that repetition here is unnecessary (Renal Tuberculosis, p. 1487). The use of cystoscopy, x-ray, and other diagnostic measures differs in no way from their employment in adults with the exception that special, small-caliber instruments are necessary for young children.

Prognosis. In infants and young children, in whom renal tuberculosis is commonly part of a generalized miliary tuberculosis, the mortality is very high. In unilateral tuberculosis of the kidney in children, early nephrectomy results in arrest and cure in a considerable percentage of cases. However, most authors believe that one should be even more guarded in the prognosis of renal tuberculosis in children than in adults, since in the former there is greater likelihood of recurrence and general dissemination of the disease following nephrectomy. This increases in proportion to the youth of the patient.

Treatment. The treatment of chronic renal tuberculosis in children and adolescents is essentially the same as in adults. The treatment of unilateral lesions is early nephrectomy with adequate after-care. Bilateral lesions are more frequent in children than in adults. As a rule,

these cases are treated medically; but if one kidney is pyonephrotic and functionless and the function of the other is adequate to sustain life, removal of the badly diseased kidney is indicated. Because of the greater tendency to recurrence and rapid dissemination in young children, a very careful preoperative examination for extraurinary active tuberculosis, as well as examination of the opposite kidney, must be made before advising nephrectomy.

The postoperative care is most important. It should be remembered that in children the pulmonary focus is apt to be more in evidence than is the case in the adult. Heliotherapy, and proper hygienic, dietary, and medical treatment are essential, and are described under Treatment of Postoperative and Inoperable Urogenital Tuberculosis (p. 1196).

Renal Cysts: Polycystic Disease. Cystic conditions of the kidney in children are decidedly uncommon. Numerous instances of still-births are on record where delivery was impeded because of enormous cysts of the kidneys; but records of renal cysts occurring in regular pediatric practice are rare. In a study of 4,903 autopsies upon infants carried out at the Babies' Hospital, New York, 19 cases of cystic kidney were discovered; 15 of these were classed as small cysts, 2 as large cysts, and 3 as cysts and hydronephrosis. Eleven cases corresponded to the typical polycystic kidney, but the remaining 8 were apparently unilateral or otherwise different from the accepted form of congenital polycystic disease.

Polycystic kidneys are occasionally observed in infancy, but such infants usually die within a few months of birth. When the disease is compatible with life, signs and symptoms leading to its discovery are not manifest, as a rule, until early middle life. However, children harboring congenitally cystic kidneys are often thin, pale, and definitely below par. They are usually considered cases of nephritis, as indeed they are, and the polycystic condition is rarely discovered until adult life. In our personal experience there has been only 1 case—that of a 9-year-old boy—in which the diagnosis was made in childhood; here hematuria was the symptom which led to a complete urological investigation.

Other types of renal cysts (solitary, multiple, and multilocular) are very rare, and most of the reported cases have been postmortem or operative findings. Single or multiple cysts of varying sizes are occasionally seen in association with nephritis, hydronephrosis, or tuberculosis. What has been said regarding cystic conditions of the adult kidney applies also to the condition in childhood.

Movable Kidney. Nephroptosis in children is almost unheard of, and presents no clinical problem.

Renal Calculus. The incidence of renal calculus in infants and children is low, the condition being about half as common as renal tuberculosis. Boys are affected more often than girls. As a rule, the calculous disease is confined to the kidney, but in a small percentage of cases affects the ureter and bladder as well. Steady improvement in dietary conditions among infants and children has markedly decreased the incidence of urinary stone in the first decade of life in the United States.

Pathology. In early cases, pathological changes are slight. Late cases, complicated by obstruction and infection, will show hydronephrosis, pyelonephritis, and pyonephrosis.

Calcium oxalate stones predominate in the kidneys of children, with the calcium phosphate variety next in number.

Symptoms and Diagnosis. Abdominal pain, localized in the flank on the affected side, and varying from a dull ache to severe colicky pain, is the predominant symptom, being present in almost every case. Urinary symptoms are not outstanding except in cases of long duration and associated with infection or complicated by ureteral or vesical calculi. Fever is also infrequent except in cases with obstruction and infection.

Tenderness in the flank on the affected side is commonly present. The kidney may be enlarged and tender.

In early cases, hematuria and pyuria are usually absent; in cases of long standing, particularly those presenting ureteral and bladder calculi as well, the urine will show varying amounts of pus and blood. Cultures are usually negative in early cases; but in cases of long standing the *Bacillus proteus* is found relatively often.

The diagnosis of renal calculus in children is quite simple. Even in very young children, it should follow the usual routine urological examination, namely: (1) history, (2) physical examination, (3) examination of the urine, (4) retrograde pyelography, with its attendant estimations of bilateral renal function and infection.

A history of colicky pain in the flank, with or without disturbances of urination, should suggest a plain x-ray of the urinary tract plus cystoscopic and pyelographic studies.

A plain x-ray plate will usually disclose the presence of renal calculus.

Non-shadow-casting calculi, such as cystine and uric acid stones, will generally be identified by filling defects in the pyelogram; these are uncommon in children. In long-standing cases, pyelographic evidence of

obstructive and infective changes in the renal pelvis and calyces will be observed. Depending on the site of the obstruction, the pyelogram will show dilatation of the renal pelvis, widening of the infundibular areas, and enlargement and blunting of the calyces.

Treatment. The treatment of renal calculus is surgical. At any age surgical intervention should be immediate if obstruction and infection are present. Operation in young children may be postponed until their fourth year if the calculi are small and obstruction and infection are absent.

RECURRENCE: POSTOPERATIVE CARE. Recurrences following removal of renal stones are fairly common in children, as in adults. In recurrent cases, the *Bacillus proteus* is not infrequently present.

Patients should be under observation for at least 3 years following operation. The postoperative treatment, to prevent recurrence, is essentially the same as that prescribed for adults.

A plain x-ray of the urinary tract should be taken at the time of the patient's discharge from the hospital and again in 6 months. Following this, annual x-rays should be taken for as long as seems necessary.

Renal Tumors. Renal tumors, in children, with the exception of the so-called Wilms' tumor, are exceedingly rare. The Wilms' tumor, while not common, occurs sufficiently often to present an important clinical problem, and has been the subject of an extensive literature in recent years. This lesion has been considered in some detail under Tumors of the Renal Parenchyma (p. 1553).

BIBLIOGRAPHY

- ABESHOUSE, B. S. Rupture of the kidney pelvis. *Surg. Gynec. & Obst.*, 60: 710, 1935.
- ADAMS, PAYSON, AND HUNT, H. B. Wilms' tumor. *Trans. S. Central Section of A. U. A.*, 1939.
- ADDIS, T., AND LEW, W.: Diet and death in acute uremia. *J. Clin. Invest.*, 18: 773, 1939.
- ADDIS, THOMAS, AND OLIVER, J. R. The renal lesions in Bright's disease. N. Y., P. B. Hoeber, 1931.
- ADDISON, O. L.: Tuberculosis of the kidney in childhood. *Brit. M. J.*, 2: 565, 1935.
- ALBARRAN, J., AND IMBERT, L.: Les tumeurs du rein. Paris, Masson et Cie, 1905.
- ALBRIGHT, F., et al.: Renal complications of hyperparathyroidism. Studies on the physiology of the parathyroid glands. *Am. J. Med. Sci.*, 187: 49, 1934.
- ALBRIGHT, F., AND BLOOMBERG, E.: Hyperparathyroidism and renal disease, with a note as to the formation of calcium casts in this disease. *Trans. Am. Assoc. Genito-Urin. Surg.*, 27: 195, 1934.
- ALBRIGHT, F., AND BLOOMBERG, E.: Hyperparathyroidism and renal disease. *J. Urol.*, 34: 1, 1935.
- ALBRIGHT, F., SELKOWITZ, H., AND CHUTE, R.: Non-surgical aspects of the kidney stone problem. *J. A. M. A.*, 113: 2049, 1939.

- ALTNOW, H. O., VAN WINKLE, C. C., AND COHEN, S. S.: Renal amyloidosis: a further study of the clinical course and pathological lesions in 57 cases. *Arch. Int. Med.*, 63: 249, 1939.
- ALYEA, E. P.: Medullablastoma involving the kidney. *Southern Med. J.*, 26: 753, 1933.
- ANDERSON, W. A. D.: Hyperparathyroidism and renal disease. *Arch. Path.*, 27: 753, 1939.
- BAEHR, G.: The nature of glomerulonephritis. *Bull. N. Y. Acad. Med.*, 14: 53, 1938.
- BAILEY, O. T., AND HARRISON, J. H.: Large benign neoplasms; pathology and clinical behavior, with report of 5 cases. *J. Urol.*, 38: 509, 1937.
- BAKER, B. M., JR.: The relation of syphilis to nephritis. *Bull. Johns Hopkins Hosp.*, 65: 196, 1939.
- BAND, DAVID: Renal tuberculosis. *Edinburgh M. J.*, 42: 175, 1935.
- BARETZ, L. H.: Rupture of the kidney following pyelography. *J. A. M. A.*, 106: 980, 1936.
- BARNEY, J. D.: Recurrent renal calculi. *Boston M. & S. J.*, 186: 9, 1922.
- BARNEY, J. D.: Gonococcal infections of the kidney. *J. Urol.*, 9: 79, 1923.
- BARNEY, J. D.: Hemorrhagic cyst of the kidney. *J. Urol.*, 36: 602, 1936.
- BARNEY, J. D., AND MINTZ, E. R.: Some newer conceptions of urinary stone formation. *Trans. Am. Assoc. Genito-Urin. Surg.*, 27: 203, 1934.
- BARNEY, J. D., AND SULKOWITZ, H. W.: Progress in the management of urinary calculi. *J. Urol.*, 37: 746, 1937.
- BARRINGER, B. S.: Roentgen therapy (especially of Wilms' tumors). *J. Mt. Sinai Hosp.*, 4: 705, March-April 1938.
- BAZY, P.: Hydronephrose. *Encycloped. franc. d'urolog.*, 3: 150, 1914 (O. Doin et Fils, Paris).
- BEACH, E. W., AND SCHULTZ, W. S.: Spontaneous healing in renal tuberculosis. *J. Urol.*, 46: 590, 1941.
- BEER, EDWIN: Leukoplakia of the pelvis of the kidney and its diagnosis. *Am. J. Med. Sci.*, 147: 244, 1914.
- BEER, EDWIN: Cystine nephrolithiasis, colon bacillemia. *Internat. J. Surg.*, 33: 219, 1920.
- BEER, EDWIN: Perinephritic abscess. *J. A. M. A.*, 90: 1375, 1928.
- BEER, EDWIN: Cocci infections of the renal cortex. *J. A. M. A.*, 106: 1063, 1936. Also: *J. Urol.*, 35: 491, 1936.
- BEER, EDWIN: Some aspects of malignant tumors of the kidney. *Surg. Gynec. Obst.*, 65: 433, 1937.
- BEER, EDWIN, AND EDELMAN, LEO: Delayed wound healing following nephrectomy for tuberculosis. *Ann. Surg.*, 104: 748, 1936.
- BELL, E. T.: The early stages of glomerulonephritis. *Am. J. Path.*, 12: 801, 1936.
- BELL, E. T.: A classification of renal tumors with observation on the frequency of the various types. *J. Urol.*, 39: 238, 1938.
- BENEVENTI, F. A.: Hydrocalyx: its relief by retrograde dilatation. *Am. J. Surg.*, 41: 244, 1943.
- BENNETT, S. H. B.: *Aerogenes capsulatus* in the urine. *Practitioner*, 9: 92, 1917.
- BEREGOFF, P.: Renal actinomycosis, with particular reference to the urinary findings. *Michigan State J. M.*, 28: 383, 1929.
- BERGMAN, H. C., AND DRURY, D. R.: A study of acute renal insufficiency. *J. Clin. Invest.*, 18: 777, 1939.
- BERNSTEIN, A.: Pyelitis complicating pregnancy. *Urol. & Cutan. Rev.*, 42: 45, 1938.
- BIRCH-HIRSCHFELD, F. V.: *Centralb. f. d. Krankh. d. Harn-u. Sex. Org.*, 5: 97, 1894.
- BIRKHAUG, K. E., AND PARLOW, A. L.: Gonococcal infection of the kidney. *J. Urol.*, 20: 83, 1928.
- BLUMER, GEORGE: Pyuria in typhoid fever. *Johns Hopkins Hosp. Rpts.*, 5: 327, 1895.
- BOYD, C. H., AND LEWIS, L. G.: Nephrectomy for arterial hypertension. *J. Urol.*, 39: 627, 1938.

- BOYD, M. L.: Formation of renal calculi in bedridden patients. *J. A. M. A.*, 116: 2245, 1941.
- BRAASCH, W. F.: Perinephritic abscess. *Surg. Gynec. & Obst.*, 21: 631, 1915.
- BRAASCH, W. F.: Lesions of the nerves of the urinary tract. *J. Urol.*, 13: 383, 1925.
- BRAASCH, W. F.: Clinical data concerning chronic pyelonephritis. *J. Urol.*, 39: 1, 1938.
- BRAASCH, W. F.: Renal disease as a factor in hypertension. *Am. J. Surg.*, 56: 209, 1942.
- BRAASCH, W. F., AND SCHACHT, F. W.: Pathological and clinical data concerning polycystic kidney. *Surg. Gynec. & Obst.*, 57: 467, 1933.
- BRAASCH, W. F., AND SUTTON, E. B.: Prognosis in bilateral renal tuberculosis. *J. Urol.*, 46: 567, 1941.
- BRADLEY, J. E., AND PINCOFFS, M. C.: Association of adeno-myo-sarcoma (Wilms' tumor) with arterial hypertension. *Ann. Int. Med.*, 11: 1613, March 1938.
- BRADY, LEO: Carbuncles of the kidney (metastatic staphylococcus abscess of the kidney cortex). *J. Urol.*, 27: 295, 1932.
- BRAND, ERWIN, BLOCK, R. J., AND CAHILL, G. F.: Cystinuria VI: The metabolism of the hydroxy-analogue of methionine. *J. Biol. Chem.*, 119: 681, 1937.
- BRAND, ERWIN, BLOCK, R. J., AND CAHILL, G. F.: Cystinuria VII: the metabolism of S-methylcysteine of γ -thio-butyric acid and of γ , γ' -Dithiodibutyric acid. *J. Biol. Chem.*, 119: 689, 1937.
- BRAND, ERWIN, BLOCK, R. J., KASSELL, B., AND CAHILL, G. F.: Carboxy-methylcysteine metabolism, its implications on therapy in cystinuria and on the methionine-cysteine relationship. *Proc. Soc. Exp. Biol. and Med.*, 35: 501, 1936.
- BRAND, ERWIN, BLOCK, R. J., KASSELL, B., AND CAHILL, G. F.: Cystinuria V: the metabolism of casein and latalbumin. *J. Biol. Chem.*, 119: 669, 1937.
- BRAND, ERWIN, AND CAHILL, G. F.: Further studies on metabolism of sulphur compounds in cystinuria. *Proc. Soc. Exp. Biol. and Med.*, 31: 1247, 1934.
- BRAND, ERWIN, CAHILL, G. F., AND BLOCK, R. J.: Cystinuria IV. the metabolism of homocysteine and homocystine. *J. Biol. Chem.*, 110: 399, 1935.
- BRAND, ERWIN, CAHILL, G. F., AND HARRIS, MEYER M.: Metabolism of various sulphur compounds in cystinuria. *Proc. Soc. Exp. Biol. and Med.*, 31: 348, 1933-34.
- BRAND, ERWIN, CAHILL, G. F., AND HARRIS, MEYER M.: Cystinuria II: the metabolism of cystine, cysteine, methionine, and glutathione. *J. Biol. Chem.*, 109: 69, 1935.
- BROWN, A. E.: Hyperparathyroidism with nephrolithiasis. *Proc. Staff Mtg., Mayo Clinic*, 10: 417, 1935.
- BROWN, R.: Spontaneous rupture of the renal pelvis. *Surg. Clin. North Am.*, 10: 969, 1930.
- BUGBEE, H. G.: Leiomyoma of the kidney. *J. Urol.*, 21: 363, 1929.
- BUGBEE, H. G.: Clinical aspects of calculus disease. *Bull. N. Y. Acad. Med.*, 14: 105, 1938.
- BUMPUS, H. C., JR., AND THOMPSON, G. J.: Renal tuberculosis: changing conceptions in decade 1920-1930. *Am. J. Surg.*, 9: 545, 1930.
- BUSSE, O.: *Virchow's Arch. f. path. Anat.*, 157: 346, 1899.
- CABOT, HUGH: Blood-stream infections of the kidney. *Brit. J. Urol.*, 8: 233, 1936.
- CABOT, H., AND BUCHTEL, H. A.: Pyelonephritis. *Surg. Clin. North Am.*, 17: 1161, 1937.
- CABOT, H., AND CRABTREE, E. G.: Frequency of recurrence of stone in the kidney after operation. *Surg. Gynec. & Obst.*, 24: 1, 1917.
- CAHILL, G. F.: Adrenogenital syndrome and adrenocortical tumors. *New Eng. J. Med.*, 218: 803, May 1938.
- CAHILL, G. F., *et al.*: Adrenal cortical tumors. *Surg. Gynec. Obst.*, 62: 287, 1936.
- CAHILL, G. F., *et al.*: Adrenal cortical tumors. *Surg. Gynec. & Obst.*, 74: 281, 1942.
- CAHILL, G. F., AND FISH, G. W.: Surgical aspect of polycystic kidney disease. *Trans. Am. Assoc. Genito-Urin. Surgeons*, 34: 81, 1941.
- CAIRNS, H. W. B.: Heredity in polycystic disease of the kidneys. *Quart. J. Med.*, 18: 359, 1925.

- CALDER, R. M., AND PORRO, F. W.: Adenoma of adrenal cortex simulating pituitary basophilism (Cushing's syndrome). *Bull. Johns Hopkins Hosp.*, 57: 99, 1935.
- CALLANDER, C. L., *et al*: Gas gangrene; analysis of 109 cases encountered in civil practice. *Am. J. Surg.*, 42: 811, 1933.
- CAMERON, J. D. S.: Protein in the treatment of nephritis. *Edinburgh M. J.*, 46: 386, 1939.
- CAMPBELL, M. F.: Renal carbuncle in infancy. *J. A. M. A.*, 98: 1729, 1932.
- CAMPBELL, M. F.: Renal tuberculosis in juveniles. *Am. J. Dis. Child.*, 45: 555, 1933.
- CAMPBELL, M. F.: Primary malignant tumors of the urogenital tract in infants and children. *J. A. M. A.*, 109: 20, 1937.
- CARSON, W. J.: Ureteral dilatation of pregnancy; autopsy findings. *J. Urol.*, 16: 167, 1926.
- CARSON, W. J.: Bilateral aneurysm of the renal artery. *Am. J. Surg.*, 6: 103, 1929.
- CARSON, W. J.: Ascending urinary infection. *Arch. Surg.*, 23: 74, 1931.
- CARY, M. K.: The racial incidence of urolithiasis. *J. Urol.*, 37: 651, 1937.
- CASONI, T.: La diagnosi biologica dell' echinococci umana mediante l'intradermoreazione. *Folia Clin. Chim. et Micros.*, p. 4, 5-16, 1912.
- CAULK, J. R.: Renal tuberculosis. *J. Urol.*, 6: 97, 1921.
- CAULK, J. R.: X-ray in the diagnosis of polycystic kidney. *Radiology*, 20: 488, 1933.
- CAULK, J. R.: Tumors of the renal pelvis and ureter. *Ann. Surg.*, 106: 68, 1937.
- CHAUVIN, E.: Dégénérescence polykystique bilatérale du rein diagnostiquée cliniquement. *Ann. d. Mal. d. reins*, 8: 215, 1934.
- CHOWN, B., AND LEE, M.: Renal rickets and dwarfism in pituitary disease. *Am. J. Dis. Child.*, 53: 117, 1937.
- CHRISTIAN, H. A.: Types of nephritis and their management. *J. A. M. A.*, 102: 169, 1934.
- CHURCH, CYRIL K.: Nephroptosis: review of literature and an analysis of palliative or operative treatment in 266 cases of primary nephroptosis. *Am. J. Surg.*, 34: 41, 1936.
- CHURCHILL, E. D., AND COPE, OLIVER: Surgical treatment of hyperparathyroidism. *Anz. Surg.*, 104: 4, 1936.
- CHUTE, RICHARD: The vital importance of the relation of hyperparathyroidism to the formation of certain urinary calculi—and its remedy. *New England J. Med.*, 210: 1251, 1934.
- CHUTE, RICHARD: The significance of urea-splitting bacteria in the formation of urinary calculi. *New Engl. M. J.*, 219: 1030, 1938.
- CHUTE, RICHARD: Clinical aspects of hyperparathyroidism. *J. Urol.*, 41: 762, May 1939.
- COHNHEIM, J.: Virchow's *Arch. f. path. Anat.*, 65: 64, 1875.
- COLBY, F.: Urinary calculi associated with parathyroid disease. *Surg. Gynec. Obst.*, 59: 210, 1934.
- COLSTON, J. A. C.: Calcified cyst of the kidney. *Bull. Johns Hopkins Hosp.*, 51: 125, 1932.
- COLSTON, J. A. C., AND BAKER, W. W.: Late effects of various types of trauma to the kidneys. *Arch. Surg.*, 34: 99, 1937.
- CONTHADES, X. J.: Étude radioscopique de la stase urinaire gravidique par l'uretéro-pyélographie ascendante. *Gynec. et Obstet.*, 35: 32, 1937.
- COOK, E. N.: Infections of the urinary tract of obscure etiology. *J. Urol.*, 36: 460, 1936.
- CORBUS, B. C., AND DANFORTH, W. C.: Pyelitis in pregnancy. *J. Urol.*, 18: 543, 1927.
- CORCORAN, A. C., AND PAGE, I. H.: Arterial hypertension: correlation of clinical and experimental observations. *J. A. M. A.*, 116: 690, 1941.
- CORCORAN, A. C., AND PAGE, I. H.: Renal blood-flow in experimental renal hypertension. *Am. J. Physiol.*, 135: 361, 1942.
- COUNSELLER, V. S., AND MELVILLE, J. G.: Leiomyoma associated with benign cysts in kidney with duplicate pelves. *J. Urol.*, 35: 253, March 1936.

- COUNSELLER, V. S., AND PRIESTLY, J. T.. The present conception of renal lithiasis. *J. A. M. A.*, 104: 1309, 1935
- CRABTREE, E. G.: Observations on the etiology of renal infections. *Lancet-Clinic*, 116: 96, 1916.
- CRABTREE, E. G.: Hydronephrosis of pregnancy. *J. Urol.*, 38: 605, 1937
- CRABTREE, E. G., AND PRATHER, G. C. Urinary diseases in pregnancy. *J. Urol.*, 26: 499, 1931.
- CRABTREE, E. J., AND REID, D. E. Pregnancy pyelonephritis in relation to renal damage and hypertension. *Am. J. Obst. Gynec.*, 40: 17, 1940.
- CRABTREE, E. G., AND SHEDDEN, W. M. Sagging kidney as a factor in the persistence of colon bacillus pyelitis. *J. Urol.*, 6: 207, 1921
- CRAIG, C. F., AND FAUST, E. C.. Clinical parasitology. Chapt. 23, The Cyclophillidean Tapeworms of Man, pp 461-474, Phila., Lea & Febiger, 1937.
- CRAIG, G., AND LEE-BROWN, R. K. Hydatid disease of the kidney. *Surg. Gynec. & Obst.*, 46: 668, 1928.
- CRANWELL, D. J., AND HERRERA-VEGAS, M. Tratamiento de los quistes hidatico. Buenos Aires, C. Hermanos, 1910
- CROSBIE, A. H., AND PINKERTON, H. Malignant leiomyoma of the kidney. *J. Urol.*, 28: 27, 1932.
- CROWELL, C. C. Squamous cell carcinoma of the renal pelvis. *Proc. Inst. Med., Chicago*, 13: 90, 1940
- CULVER, HARRY: Replacement lipomatosis of the kidney. *Surg. Clin. N. A.*, 14: 813, 1934
- CUMMING, R. E. Polycystic disease. *J. Urol.*, 30: 149, 1928
- CUMMING, R. E., AND NELSON, R. J. Actinomycosis of the urinary tract. *Surg. Gynec. & Obst.*, 49: 352, 1929
- CUNNINGHAM, J. H. Large solitary and multiple cysts of the kidney. *Surg. Gynec. & Obst.*, 23: 698, 1916
- DANIEL, W. E.: The hypertensive factors in Wilms' tumor. *Southern M. J.*, 32: 1014, October 1939
- DAVIDSON, O. W.. The relationship of renal calculi to hyperparathyroidism. *J. Urol.*, 37: 35, 1937.
- DAVIS, JAMES E.: Congenital polycystic kidneys. *Am. J. Obst. & Gynec.*, 9: 758, 1925
- DAY, R. V. Renal tuberculosis. Why clinically established renal tuberculosis never completely heals. *Calif. & West Med.*, 37: 217, 1932.
- DEAN, A. L., JR. Management of renal tumors. *Bull. New York Acad. Med.*, 14: 128, 1938.
- DEAN, A. L., JR.: Radiation therapy of tumors of parenchyma in adults. *J. Urol.*, 39: 303, March 1938.
- DEAN, A. L., JR., AND PACK, G. T.: Embryonal adenocarcinoma of the kidney. *J. A. M. A.*, 98: 10, 1932.
- DELZELL, W. R., AND HARRAH, F. W.. Eleven cases of ruptured kidney. *J. Urol.*, 19: 131, 1928.
- DEMING, CLYDE, L.: Nephroptosis: causes, relation to other viscera, and correction by a new operation. *J. A. M. A.*, 95: 251, 1930. Also: *Am. J. Surg.*, 9: 218, 1930.
- DEMING, CLYDE, L.: Sarcoma of the kidney cured. *New England J. Med.*, 199: 273, 1928
- D'ESCRIVAN, ROGER: Contribution à l'étude des tuberculoses rénales bilatérales. Thèse de Paris, No 418, 1937.
- DETARNOVSKY, G. Primary echinococcus cyst of the kidney. *Surg. Clin. North Am.*, 7: 783, 1927.
- DEW, H. R.: Some aspects of echinococcus disease. *Surg.* 2: 353, 1937.
- DOERING, A.: Beiträge zur Nierenchirurgie. *Deutsche Ztschr. f. Chir.*, 87: 32, 1907

- DOMANSKY, T. J.: Renal calculi: new method for qualitative analysis. *J. Urol.*, 37: 399, 1937.
- DOWLING, G. B.: Syphilitic nephritis. *Guy's Hosp. Rpts.*, 77: 454, July-October 1927.
- DUNGER, R.: Zur lehre von der cystenniere, mit besonderer berücksichtigung ihrer heredität. *Ziegler's beitrage z. path. Anat. u. allg. Path.*, 35: 445, 1904.
- EBERBACH, C. W.: The pathogenesis of renal tuberculosis. *J. Urol.*, 17: 233, 1927.
- EBERTH, C. J.: *Virchow's Arch. f. path. Anat.*, 55: 518, 1872.
- EISENDRATH, D. N.: Ureteral stricture and hydronephrosis as late sequels of kidney injuries. *J. A. M. A.*, 104: 1898, 1935.
- EKEHORN, G.: Ueber die frequenz der nierentuberkulose im verhaeltniss zum alter und geschlecht der patienten. *Deutsche med. Wchnschr.*, 52: 615, 1926.
- ELIASON, E. L., *et al.*: *Clostridium welchii* and associated organisms. *Surg. Gynec. & Obst.*, 64: 1005, 1937.
- ELLIS, A., AND EVANS, H.: Renal dwarfism. *Quart. J. Med.*, 2: 231, 1933.
- ELWARD, J. F., AND SPIRE, R. L.: Bilateral hypernephroma. *Radiol.*, 35: 274, 1940.
- ELWYN, HARMAN: Nephritis. *N. Y., The Macmillan Co.*, 1928. Also: *Cyclopedia Med.* 2: 763-853, Phila., 1933.
- EWING, J.: *Neoplastic diseases*, Ed. 3. Phila., W. B. Saunders Co., 1934.
- EZICKSON, W. J., AND GREENE, L. B.: Solitary cyst of the kidney associated with adenocarcinoma of the walls of the cyst. *J. Urol.*, 38: 153, 1937.
- FAIRLEY, N. H.: The complement-fixation test for hydatid disease and its clinical value. *Med. J. Australia*, 1: 341, 1922.
- FALCI, E.: Tuberculose rénale de l'enfant (fréquence, evolution, pronostic) comparée à celle de l'adulte. *J. d'uro.*, 20: 301, 1925.
- FARR, L. E., AND VAN SLYKE, D. D.: Relation between plasma protein level and edema in nephrotic children. *Am. J. Dis. Child.*, 57: 306, 1939.
- FERRIER, P. A., AND BLISS, W. P.: Pyelolithotomy complicated by gas bacillus infection originating in a renal calculus. *J. Urol.*, 20: 471, 1928.
- FISH, GEORGE W.: Large solitary cysts of the kidney. *J. A. M. A.*, 112: 514, February 11, 1939.
- FISH, GEORGE W., AND HAZZARD, CHARLES T.: Nephroptosis. *J. Urol.*, 41: 336, 1939.
- FISHBERG, A. M.: Hypertension and Nephritis. Ed. 4. Phila., Lea & Febiger, 1939.
- FLEXNER, S.: Certain forms of infection in typhoid fever. *Johns Hopkins Hosp. Rpts.*, 5: 343, 1895.
- FLOCKS, R. H.: Calcium and phosphorus excretion in the urine of patients with renal or ureteral calculi. Therapeutic and etiologic considerations. Presented before the Section on Urology, A. M. A., St. Louis, Mo., May 19, 1939 (to be published).
- FORSYTHE, W. E.: Bilateral hypernephroma: report of a case. *J. Urol.*, 47: 784, 1942.
- FORTUNATO, M.: Le lesioni renali nelle infezioni attenuate da bacillo perfringens. *Riv. di path. spir.*, 16: 439, 1936.
- FOWLER, R. S.: Simple serous cysts of the kidney. *N. Y. Med. J.*, 94: 1109, 1911.
- FRASER, JOHN: Adeno-sarcomatous tumours of the kidney; a clinico-pathological study. *Edinburgh Med. J.*, 24: 372, 1920.
- FREW, R. S.: On carcinoma originating in the suprarenal medulla in children. *Quart. J. Med.*, 4: 123, 1914.
- FRIEDMAN, B., *et al.*: Unilateral renal disease and hypertension, etc. *J. Urol.*, 48: 5, 1912.
- FRÖBOESE, C.: Seltene formen der angeborenen frühsyphilitischen eberentzündung (einschliesslich einer kurzen bermerkung zur frage der syphilitischen merentzündung). *Frankfurt. Ztschr. f. Path.*, 52: 603, 1938.
- FUJIMAKI, Y.: Formation of urinary and bile duct calculi in animals fed on experimental rations: note on treatment. *Japan Med. World*, 6: 29, 1926.

- GARCEAU, E.: Renal, ureteral, perirenal and adrenal tumors, and actinomycosis and echinococcus of the kidney. N. Y., D. Appleton & Co.
- GEISINGER, J. F.: The cystic kidney. *J. Urol.*, 34: 202, 1935.
- GERAGHTY, J. T., AND FRONTZ, W. A.: A study of primary hydronephrosis. *J. Urol.*, 2: 161, 1918.
- GERAGHTY, J. T., SHORT, J. T., AND SCHANZ, R. F.: Multiple renal calculi; unilateral and bilateral. *J. A. M. A.*, 77: 901, 1921.
- GERARD, M.: Contusions rénales et leurs suites éloignées. *Echo méd. du nord* 34: 557, 1930.
- GESCHICKTER, C. F.: Suprarenal tumors. *Am. J. Cancer*, 23: 105, 1935.
- GESCHICKTER, C. F., AND WIDENHORN, H.: Nephrogenic tumors (Wilms' tumors, cystadenoma, and hypernephroma). *Am. J. Cancer*, 22: 620, 1934.
- GIBSON, T. E.: Nephrectomy versus autonephrectomy in renal tuberculosis. *J. Urol.*, 33: 145, 1935.
- GIBSON, T. E.: Problems in surgical treatment of renal calculi. *Arch. Surg.*, 37: 211, 1938.
- GILBERT, J. B.: Diagnosis and treatment of malignant renal tumors: historical data. *J. Urol.*, 39: 223, 1938.
- GILBERT, J. B., AND MACMILLAN, S. F.: Cancer of the kidney. Squamous-cell carcinoma of the kidney pelvis, with special reference to etiology. *Ann. Surg.*, 100: 429, 1935.
- GOEBEL, C.: Ueber den bacillus der schaumorgane. *Centralh. f. allg. Path.*, 6: 465, 1895.
- GOLDBLATT, HARRY, *et al.*: Experimental observations on the surgical treatment of hypertension. *Surgery*, 4: 480, 1938.
- GOLDSTEIN, A. E., AND ABESHOUSE, B. S.: Gas-bacillus infections in urology. *J. Urol.*, 31: 547, 1934.
- GOLDSTEIN, A. E., AND ABESHOUSE, B. S.: Urinary calculi in bone diseases: review of literature and report of cases. *Arch. Surg.*, 31: 943, 1935.
- GOLDSTEIN, A. E., AND OSTRO, M.: Roentgenological diagnosis of perinephritic abscess and perinephritis. *Am. J. Roent.*, 11: 371, 1938.
- GOOD, L. P.: Actinomycosis of the abdomen. *Arch. Surg.*, 22: 307, 1931.
- GORDON-TAYLOR, G.: Gigantic benign tumor weighing 22 pounds; nephrectomy; cure. *Brit. J. Surg.*, 17: 551, 1930.
- GRAVES, R. C.: Congenital solitary kidney with large solitary cyst. *J. Urol.*, 23: 555, 1930.
- GRAVES, R. C., AND PARKINS, L. E.: Carbuncle of the kidney. *J. Urol.*, 35: 1, 1936.
- GRAWITZ, P.: Die sogenannten lipome der niere. *Arch. f. path. Anat. u. f. Klin. Med.*, 93: 39, 1883.
- GREEN, D. F., MORRIS, M. L., CAHILL, G. F., AND BRAND, ERWIN. Canine cystinuria, II: Analysis of cystine calculi and sulfur distribution in the urine. *J. Biol. Chem.* 114: 91, 1936.
- GROSSMAN, E. B., AND WILLIAMS, J. R., JR.: Relation of age to renal pressor substance. *Arch. Int. Med.*, 62: 799, 1938.
- HAGER, B. H.: A contribution to the etiology of calcareous pyelonephritis. *J. Urol.*, 15: 133, 1926.
- HAGER, B. H., AND MACARTH, T. B.: Four cases of urinary calculi from which proteus ammoniac was isolated. *Med. Clin. North Am.*, 10: 693, 1926.
- HAMER, H. G.: Diagnosis and treatment of metastatic renal infection. *J. Urol.*, 38: 530, 1937.
- HAND, J. R., AND BRODERS, A. C.: Carcinoma of the kidney: the degree of malignancy in relation to factors bearing on prognosis. *J. Urol.*, 28: 199, 1932.
- HARRAH, F. W.: Embryonal sarcoma of the kidney in children: 2 cases. *J. Urol.*, 29: 445, 1933.
- HARRIS, HARRY, AND HARRIS, R. G. S.: Renal sympathetico-tonus, renal pain and renal sympathectomy. *Brit. J. Urol.*, 2: 367, 1930.

- HARRIS, R. I.: Observations on the pathology of surgical tuberculosis. with particular reference to the incidence of renal bacilluria. *Am J. Surg.* 10: 514, 1930.
- HARRISON, J. H.: Trauma to the kidney. *Surg. Gynec. & Obst.*, 70: 93, January 1940.
- HARVIER, P., *et al.*: Nephrite urémique consécutive à une septicémie à perfringens post abortus. *Bull et mem Soc méd d. hôp de Paris*, 1: 691, 1934.
- HAYWARD, W. G.: Malignant papillary cystadenoma of the kidney. *J. Urol.*, 44: 259, 1940.
- HELMER, O. M., AND PAGE, I. H.: Purification and some properties of renin. *J. Biol. Chem.*, 127: 757, 1939.
- HELMHOLZ, H. T.: Spontaneous pyelitis in the rabbit and ascending infection of the urinary tract; its relationship to this disease in man. *Surg. Gynec. & Obst.*, 55: 449, 1932.
- HENLINE, R. B.: Spontaneous rupture of the kidney. *J. A. M. A.*, 83: 1411, 1924.
- HENLINE, R. B.: Renal tuberculosis, diagnosis and treatment, with a study of 97 cases of nephrectomy for tuberculosis. *Surg. Gynec. & Obst.*, 57: 231, 1933.
- HENLINE, R. B.: Renal infections. *Urol. & Cutan. Rev.*, 40: 308, 1936.
- HENLINE, R. B., AND BRAY, J. L.: The value of serial pyelograms in hydronephrosis and nephroptosis. *J. Urol.*, 38: 620, 1937.
- HENLINE, R. B., AND BRAY, J. L.: Urogenital tuberculosis complications following diagnostic and surgical procedures. *J. Urol.*, 39: 529, 1938.
- HEPLER, A. B.: Solitary cysts of the kidney. *Surg. Gynec. & Obst.*, 1: 668, 1930.
- HEPLER, A. B.: Intrarenal changes in hydronephrosis. *J. Urol.*, 38: 593, 1937.
- HERBST, ROBERT H., AND POLKEY, H. J.: Solitary renal cysts. *J. Urol.*, 37: 490, 1937.
- HERMAN, LEON.: Chemical nephrosis. *Surg. Clinics, N. A.*, 16: 515, 1936.
- HESS, ELMER.: Diagnosis and treatment of syphilitic nephritis. *Am J. Syph.*, 11: 438, 1927.
- HESS, ELMER.: The management of the nephroptotic patient. *Urol & Cutan Rev.*, 42: 703, 1938.
- HIGGINS, C. C.: Experimental production of urinary calculi. *J. Urol.*, 29: 157, 1933. Also: *Urol & Cutan Rev.*, 38: 33, 1934; *J. A. M. A.*, 104: 1296, 1935.
- HIGGINS, C. C.: Factors which influence the formation of urinary calculi. *N. Y. State J. Med.*, 36: no 21, 1936.
- HIGGINS, C. C.: Urinary lithiasis; experimental production and solution with clinical application and end-results. *J. Urol.*, 36: 168, 1936.
- HIGGINS, C. C.: Squamous cell carcinoma of pelvis. *Arch Surg*, 38: 224, Feb 1939.
- HIGGINS, C. C., AND MENDENHALL, E. L.: Facts associated with recurrent formation of renal lithiasis, with report of new method for qualitative analysis of urinary calculi. *J. Urol.*, 42: 436, 1939.
- HINES, E. A., JR., AND LANDOR, H. H.: Factors contributing to the development of hypertension in patients suffering from renal disease. *J. A. M. A.*, 116: 1050, 1941.
- HINMAN, FRANK.: The pathogenesis of hydronephrosis. *Surg. Gynec. & Obst.*, 58: 356, 1934.
- HINMAN, FRANK.: Tuberculosis of the kidney. *Surg. Gynec. & Obst.*, 66: 329, 1938.
- HINMAN, FRANK, AND MORISON, D. M.: Comparative study of circulatory changes in hydronephrosis, caseous cavernous tuberculosis, and polycystic kidney. *J. Urol.*, 2: 131, 1924.
- HOBBS, F. B.: Elimination of tubercle bacillus by the kidneys in pulmonary tuberculosis. *Tuberc.*, 5: 57, 1923.
- HOWALD, R.: Wundgasbrand im Anschluss an Nephrectomie wegen tuberkulöser Pyonephrose. *Deutsche Ztschr. f. Chir.*, 226: 152, 1930.
- HOWARD, H. H., SUBY, H. I., AND HARBERSON, J.: Aneurysm of the renal artery. *J. Urol.*, 45: 41, 1941.
- HOWARD, T. L.: Renal rickets or renal dwarfism. *Am. J. Surg.*, 40: 323, 1938.
- HRYSZCHAK, T.: Ueber Nierenbeckenpapillome. *Ztschr. f. Urol. Chir.*, 5: 46: 1920.

- HEYNTSCHAK, T.: Operative treatment of bilateral nephrolithiasis: indications and results. *Surg. Gynec. & Obst.*, 58: 103, 1934.
- HUGGINS, C. B., AND ROOMS, N. W.: Typhoid pyonephrosis, its urological and public health significance. *J. Urol.*, 31: 587, 1934.
- HUNDLEY, J. M., *et al.*: Some physiological and pathological observations on the urinary tract during pregnancy. *Surg. Gynec. & Obst.*, 66: 350, 1938.
- HUNNER, G. L.: Ureteral strictures in obstetrics. *Aro. J. Obst.*, 9: 47, 1925.
- HUNT, V. C.: Perinephritic abscess. *J. A. M. A.*, 83: 2070, 1924.
- HUNT, V. C.: Papillary epithelioma of the renal pelvis. *J. Urol.*, 18: 225, 1927.
- HUNT, V. C., AND MAYO, C. H., 2ND. Actinomycosis of the kidney. *Ann. Surg.*, 93: 501, 1931.
- HUNT, VERNE: Bilateral hypernephroma. *Surg. Clin. North Am.*, 7: 1462, 1927.
- HUTCHINSON, R.: On suprarenal sarcoma in children with metastases in the skull. *Quart. J. Med.*, 1: 33, 1907.
- HYAMS, J. A., AND KENYON, H. R.: Localized obliterating pyelonephritis. *J. Urol.*, 46: 380, 1941.
- HYMAN, ABRAHAM. Albumin, fibrin, and bacterial stones of the urinary tract. *J. Urol.*, 19: 551, 1928.
- HYMAN, ABRAHAM: Clinical study of malignant tumors of the kidney. *Surg. Clin. North Am.*, 13: 347, 1933.
- HYMAN, ABRAHAM, AND EDELMAN, L.: Medical and surgical aspects of hematogenous infections in urology. *J. Urol.*, 28: 173, 1932.
- ILLYES, G. DE: Des calculs renaux recidivants. *J. d'urolog.*, 38: 419, 1934.
- INGRISH, G. A.: Carbuncle of the kidney: report of 10 cases. *J. Urol.*, 42: 326, 1939.
- ISRAEL, J.: *Primäre actinomycose des niere.* *Chir. Klin. d. Nierenkrankheiten*, p. 266, Berlin, August Hirschwald, 1901.
- ISRAEL, J.: Ein neuer fall von sog primärer nierenaktinomykose. *Folia Urologica*, 5: 447, 1911.
- ISRAEL, J., AND ISRAEL, W.: *Chirurgie der niere und des harnleiters.* Leipzig, 1925.
- JAMESON, E. M.: Renal tuberculosis in patients with active pulmonary tuberculosis. *Surg. Gynec. & Obst.*, 67: 56, 1938.
- JANEWAY, T.: Note on blood pressure changes following reduction of renal arterial circulation. *Proc. Soc. Exper. Biol. & Med.*, 6: 109, 1909.
- JOHNSON, C. M.: The pathogenesis of hydronephrosis. *J. Urol.*, 27: 279, 1932.
- JOHNSON, F. P. AND HILL, J. R.: Gonococcal infection of the kidney and criteria for its diagnosis. *J. Urol.*, 11: 177, 1924.
- JOLY, J. S.: Stone and calculous disease of the urinary organs. St. Louis, C. V. Mosby Co., 1931.
- JOLY, J. S.: *The etiology of stone.* *J. Urol.*, 32: 541, 1934.
- JOLY, J. S.: Anuria as a complication of lithiasis. *Tr. Am. Assoc. Genito-Urin. Surg.*, 27: 209, 1934.
- JOLY, J. S.: *The treatment of bilateral lithiasis.* *J. Mt. Sinai Hosp.*, 4: 512, 1938.
- JONES, R. W., AND ROBERTS, R. E.: Calcification, decalcification, and ossification. *Brit. J. Surg.*, 21: 461, 1934.
- JOYCE, J. L.: A study of staphylococcal disease; the renal cases. *Guy's Hosp. Rpts.*, 60: 169, 1930.
- JUDD, E. S.: Contusion and rupture of the kidney. *Collected papers.* Mayo Clinic, 9: 218, 1917.
- JUDD, E. S.: Papillary tumors of pelvis of the kidney. *Journal-Lancet*, 39: 247, 1919.
- JURASZ, A.: Movable kidney. *Proc. Roy. Soc. Med., Sect. Urol.*, 22: 13, 1928.

- KAMPMEIER, O. F.: A hitherto unrecognized mode of origin of congenital renal cysts. *Surg. Gynec. & Obst.*, 36: 203, 1923.
- KEARNS, W. M., AND TURKELTAUB, S. M.: Renal tuberculosis in children. *Wisconsin M. J.*, 31: 834, 1932.
- KELLY, H. A., AND BURNAM, C. F.: *Diseases of the kidney, ureter, and bladder*. N. Y., D. Appleton & Co., 1914.
- KELLY, H. A., AND MCCALLUM, W. G.: *Pacumaturia*. *J. A. M. A.*, 31: 375, 1898.
- KEYSER, L. D.: Etiology of urinary lithiasis; an experimental study. *Arch. Surg.*, 6: 525, 1923.
- KEYSER, L. D.: Recurrent urolithiasis: etiological factors and clinical management. *J. A. M. A.*, 104: 1299, 1935.
- KEYSER, L. D., AND BRAASCH, W. F.: Etiology of urinary lithiasis. *Internat. Abst., Surg.*, 34: 1, 1922.
- KIDD, FRANK: Acquired renal dystopia or movable kidney. *J. Urol.*, 26: 327, 1931.
- KIMBALL, F. N.: Benign papilloma of the renal pelvis. *Am. J. Surg.*, 10: 576, 1930.
- KIMBALL, F. N., AND FERRIS, H. W.: Papillomatous tumor of the renal pelvis associated with similar tumors of the ureter and bladder. *J. Urol.*, 31: 257, 1934.
- KIMBROUGH, J. C.: Surgical treatment of hydronephrosis. *J. Urol.*, 23: 97, 1935.
- KINDALL, L. B.: Rupture complications of syringe-pressure pyelograms. *Urol. & Cutan. Rev.*, 37: 711, 1933.
- KIRWIN, T. J.: Calcified renal cyst. *J. Urol.*, 15: 273, 1926.
- KNAPPER, C.: Gas gangrene from endogenic infection, etc. *Nederl. Tijdschr. v. Geneesk.*, 9: 4792, 1929.
- KRETSCHMER, H. L.: Cystinuria and cystine stones; with report of a new family of cystinurias. *Urol. & Cutan. Rev.*, 20: 1, 1916.
- KRETSCHMER, H. L.: Solitary cysts of the kidney. *J. Urol.*, 4: 567, 1920.
- KRETSCHMER, H. L.: Traumatic kidney. *Surg. Clin. North Am.*, 2: 801, 1922.
- KRETSCHMER, H. L.: Echinococcus disease of the kidney. *Surg. Gynec. & Obst.*, 36: 196, 1923.
- KRETSCHMER, H. L.: Tuberculosis of the kidney in childhood and adolescence. *Illinois M. J.*, 70: 119, 1936.
- KRETSCHMER, H. L.: Hydronephrosis in infancy and childhood. *Surg. Gynec. & Obst.*, 64: 634, 1937.
- KRETSCHMER, H. L.: Xanthine calculi: report of case and review of literature. *J. Urol.*, 38: 183, 1937.
- KRETSCHMER, H. L.: Malignant tumors of the kidney in children. *J. Urol.*, 39: 250, 1938.
- KRETSCHMER, H. L., AND BROWN, R. C.: Do alkalis used in the treatment of peptic ulcer cause kidney stones? A study of 1,940 cases. *J. A. M. A.*, 113: 1471, 1939.
- KRETSCHMER, H. L., AND DOERING, C.: Adenoma of the kidney. *Surg. Gynec. & Obst.*, 48: 629, 1929.
- KRETSCHMER, H. L., AND HEANEY, N. S.: Dilatation of the ureter and kidney pelvis during pregnancy. *J. A. M. A.*, 85: 406, 1925.
- KRETSCHMER, H. L., HEANEY, N. S., AND OCKULY, E. A.: Dilatation of the kidney pelvis and ureter during pregnancy and puerperium. *J. A. M. A.*, 101: 2025, 1933.
- KRETSCHMER, H. L., AND HIBBS, W. G.: Actinomycosis of the kidney in infancy and childhood. *J. Urol.*, 36: 123, 1936.
- KRETSCHMER, H. L., AND KANTER, A. E.: Effect of certain gynecologic lesions on the upper urinary tract: a pyelographic study. *J. A. M. A.*, 109: 1097, 1937.
- KUESTER, E.: Die tuberkulose der nieren. *Deutsche Chir. No. 52b*, vol. 2, p. 340. Stuttgart: fer. Enke, 1896-1902.

- KUTZMANN, A. A.: Leukoplakia of the renal pelvis. *Arch. Surg.*, 19: 871, 1929 (contains extensive bibliography and tabulation of all renal cases to date of publication).
- KUTZMANN, A. A.: Replacement lipomatosis of the kidney. *Surg. Gynec. & Obst.*, 52: 690, 1931.
- KUTZMANN, A. A.: Squamous cell carcinoma of pelvis with special consideration as to etiology. *J. Urol.*, 39: 487, 1938.
- LADD, W. E.: Embryoma of the kidney (Wilms' tumor). *Ann. Surg.*, 108: 885, 1938.
- LADD, W. E., AND WHITE, R. E.: Embryoma of the kidney (Wilms' tumor). *J. A. M. A.*, 117: 1858, 1941.
- LANDIS, E. M.: Hypertension and pressor activity of heated extracts of human kidneys. *Am. J. Med. Sci.*, 213: 14, 1941.
- LANGERON, L., AND LEHEAC, P.: Formes cliniques des tumeurs malignes primitives des capsules surrénales. *Ann. Méd.*, 24: 249, 1928.
- LAZARUS, J. A.: Two cases of carbuncle of the kidney. *J. Urol.*, 21: 353, 1929.
- LAZARUS, J. A.: Squamous-cell carcinoma of the renal pelvis: case with invasion of the duodenum. *J. Urol.*, 39: 34, 1938.
- LAZARUS, J. A.: Indications for surgery in polycystic kidneys. *Urol. & Cutan. Rev.*, 38: 457, 1934.
- LECOMTE, R. M.: The management of renal tumors, including cysts. *J. A. M. A.*, 105: 1963, 1935.
- LECOMTE, R. M.: Indications for operation in renal stones. *Southern M. J.*, 29: 515, 1936.
- LECOMTE, R. M.: Symptoms, diagnosis and treatment of renal cysts. *Southern Med. J.*, 31: 632, 1938.
- LEE, H. P., AND MENDER, W. F.: The effect of pregnancy on the urinary tract. *J. A. M. A.*, 102: 102, 1934.
- LEGUEU, F., AND TRUCHOT, P.: La pyelographie dans le cancer du rein. *Paris, G. Doin*, 1931.
- LEPOUTRE, C.: De la lithiase urinaire survenant chez les malades longtemps immobilisés pour diverses affections osseuses et ostéoarticulaires. *Arch. franco-belges de chir.*, 31: 789, 1928.
- LESCHER, F. G.: A comparison of pituitary basophilic syndrome and adrenal cortico-genital syndrome. *Quart. J. Med.*, 4: 23, 1935.
- LEVESQUE, J.: Deux problèmes touchant le rachitisme; rachitisme renal et rachitisme tardif. *Bull. méd. (Paris)* 53: 55, 1939.
- LIEVERTHAL, FREDERICK: Renal tuberculosis; development of the renal lesion. *Surg. Gynec. & Obst.*, 67: 26, 1938.
- LIVERMORE, G. R.: Echinococcus disease of the kidney. *Trans. Am. Assoc. Genito-Urin. Surg.*, p. 19, 1929.
- LIVERMORE, GEORGE R.: Pyelonephritis of pregnancy. *Southern Surg.*, 2: 110, 1933.
- LIVERMORE, GEORGE R.: Solitary cyst of the kidney: case. *Memphis M. J.*, 10: 13, 1935.
- LIVERMORE, G. R., BLISS, A. R., JR., AND PRATHER, E. O., JR.: Relation of vitamin A and vitamin D to urinary calculous formation. *J. Urol.*, 30: 639, 1933.
- LOEB, R. F.: Clinical aspects of nephritis. *Bull. N. Y. Acad. Med.*, 14: 65, 1938.
- LOEB, E. N. *et al*: On the permanence of recovery in acute glomerulonephritis. *J. Clin. Investigation.* 17: 623, 1938.
- LORD, F. T.: The etiology, pathogenesis and diagnosis of actinomycosis. *Med. Clin. North Am.*, 16: 892, 1933.
- LOWSLEY, O. S.: Uroselectan in urinary tuberculosis. *J. Urol.*, 25: 293, 1931.
- LOWSLEY, O. S.: Some new developments in renal surgery. *Southern M. J.*, 27: 146, 1934.
- LOWSLEY, O. S.: Experimental surgery of the kidney. *J. Kansas Med. Soc.*, 36: 397, 1935.

- LOWSLEY, O. S., AND BUTTERFIELD, P. M.: Urologic conditions among children. *J. Urol.* 16: 415, 1926.
- LOWSLEY, O. S., AND CANNON, E. M.: Aneurysm of the renal artery: report of a case. *J. A. M. A.*, 121: 1137, 1943.
- LOWSLEY, O. S., AND CURTIS, M. S.: The surgical aspects of cystic disease of the kidneys. (To be published.)
- LOWSLEY, O. S., AND HILL, T. C.: Surgical management of tuberculosis of the kidney. *N. Y. State J. Med.*, 29: 433, 1929.
- LOWSLEY, O. S., AND KIRWIN, T. J.: *Urology for Nurses*, Chapt. VI. Phila., J. B. Lippincott Co., 1936.
- LOWSLEY, O. S., AND MENNING, J. H.: Treatment of rupture of the kidney. *J. Urol.*, 45: 253, 1941.
- LUBARSCH, O. Ueber die abstammung gewisser nierengeschwuelste von embryonal abgesprengten nebennierenkeimen. *Arch. f. path. anat. u. physiol. u. f. klin. Med.*, 137: 191, 1894.
- MACKENZIE, D. W., AND HAWTHORNE, A. B.: Some studies in the distribution of blood-borne particles, including bacteria, in the kidney. *Trans. Am. Assoc. Genito-Urin. Surg.*, 21: 133, 1928.
- MACKENZIE, D. W., AND RATNER, M.: Tumors of the renal pelvis. *J. Urol.*, 28: 405, 1932.
- MACKENZIE, D. W., AND SNED, M. I.: Urological aspects of hypertension. *Surg., Gynec. & Obst.*, 70: 578, 1940.
- MACKENZIE, D. W., AND WALLACE, A. B.: The lymphatics of the lower urinary and genital tracts; an experimental study with special reference to renal infections. *J. Urol.*, 34: 516, 1935.
- MACKENZIE, D. W., AND WAUGH, T. R.: Cystadenoma pseudo-papilliferum malignum of kidney with metastases in tongue. *J. Urol.*, 18: 331, 1927.
- MAGATH, T. B.: Hydatid disease in Canada and the United States. *Am. J. Hyg.*, 25: 107, 1937.
- MAGOUN, J. A. H.: Gumma or neoplasm? Diagnostic problem. *Urol. & Cutan. Rev.*, 43: 177, March 1939.
- MAHER, C. C., AND WOSIKA, P. H.: Urologic hypertension: a study of 101 cases. *J. Urol.*, 41: 893, 1939.
- MAJOR, R. H.: Observations on the treatment of lipoid nephrosis. *Ann. Int. Med.*, 12: 1555, 1939.
- MALISOFF, J. D.: Neuroblastoma of the adrenal gland. *J. Urol.*, 41: 296, March 1939.
- MASLOW, LEO A.: Wilms' tumors: report of 3 cases and a possible fourth one in the same family. *J. Urol.*, 43: 75, January 1940.
- MATHÉ, C. P.: Carbuncle of the kidney. *Calif. & West. Med.*, 22: 601, 1924.
- MATHÉ, C. P.: Movable kidney. *Surg. Gynec. & Obst.*, 40: 605, 1925.
- MATHÉ, C. P.: The role of aberrant vessels in the production of hydronephrosis. *J. Urol.*, 19: 211, 1928.
- MATHÉ, C. P.: Spontaneous rupture of the kidney. *Urol. & Cutan. Rev.*, 36: 605, 1932.
- MATHÉ, C. P.: Aneurysm of the renal artery. *J. Urol.*, 27: 607, 1932.
- MATHÉ, C. P.: Perinephritis—suppurative and non-suppurative. *Calif. & West. Med.*, 38: 149, 1933.
- MATHÉ, C. P.: A new sign (lack of renal mobility) for diagnosis of perinephritic abscess, perinephritis, renal carbuncle, and cortical abscess. *Urol. & Cutan. Rev.*, 38: 639, 1934.
- MATHÉ, C. P.: Juvenile tuberculosis of the kidney: diagnosis and treatment. *Surg. Gynec. & Obst.*, 63: 283, 1936.

- MATHÉ, C. P.: Etiologic and pathologic considerations in juvenile renal tuberculosis. *Urol. & Cutan. Rev.*, 40: 464, 1936
- MATHÉ, C. P.: Intrinsic causes of hydronephrosis. *J. Urol.*, 38: 574, 1937
- MATHÉ, C. P.: Cancer of the kidney—present-day status of its treatment and end-results. *Calif. & West. Med.*, 46: No. 6, 1937
- MATHIFU, P.: La tuberculose rénale chez l'enfant. *Paris Méd.*, 53: 68, 1924
- MCCANN, W. S.: Bright's disease—a review of recent literature. *Arch. Int. Med.*, 65: 638, 1940
- MCCANN, W. S.: Orthostatic hypertension—effect of nephroptosis on normal renal blood supply. *J. A. M. A.*, 115: 573, 1940
- MCCARRISON, R.: Experimental production of stone in bladder. *Brit. M. J.*, 1: 717, 1927
- MCCARRISON, R.: Causation of stone in India. *Brit. Med. J.*, 1: 1009, 1931
- MCCLELLAND, J. C., AND MILLS, J. R. F.: Renal tumors. *Urol. & Cutan. Rev.*, 42: 631, 1938
- McKAY, R. W.: True aneurysm of the renal artery. *J. Urol.*, 37: 783, 1937
- McKENNA, C. M., AND KAMPMEIER, O. F.: Considerations in the development of polycystic kidney. *J. Urol.*, 32: 37, 1934
- McNULTY, P. H.: Carbuncle of the kidney—review of the literature, discussion of unilateral localized lesions of the kidney and report of case. *J. Urol.*, 35: 15, 1936
- MEDLAR, E. M.: Cases of renal infection in pulmonary tuberculosis, evidence of healed tuberculous lesions. *Am. J. Pathol.*, 2: 401, 1926
- MEDLAR, E. M.: Significance of tubercle bacilli in the urine. *Urol. & Cutan. Rev.*, 36: 71, 1932
- MEDLAR, E. M., AND SASANO, K. T.: Experimental renal tuberculosis, with special reference to excretory bacilluria. *Am. Rev. Tuberculosis*, 10: 370, 1924
- MELAND, E. L., AND BRAASCH, W. F.: Multilocular cysts of the kidney. *J. Urol.*, 29: 505, 1933
- MELCHIOR, F.: Ueber die suppurativen Nierenkompliken des Typhus, etc. *Centralbl. f. d. Grenzgeb. d. Med. u. Chir.*, 13: 689, 747, 1910
- MELEN, D. R.: Echinococcus cyst of the kidney. *J. A. M. A.*, 84: 1725, 1925
- MELENEY, F. L., HUMPHREYS, F. B., AND CARP, L.: Wound infection and catgut. *Surg. Gynec. & Obst.*, 45: 775, 1927
- MELICOW, M. M., AND GILE, H. H.: Hypermephroma in a polycystic kidney—review of literature and report of a case. *J. Urol.*, 43: 767, 1940
- MELTZER, M. L.: Papillary carcinoma of the renal pelvis. *J. Urol.*, 16: 335, 1926
- MELTZER, M. L.: Echinococcus cysts of the kidney. *J. A. M. A.*, 92: 1925, 1929
- MELVIN, P. D., AND ANDREWS, J. C.: Nephrolithiasis and cystine excretion in cystinuria. *J. Urol.*, 37: 655, 1937
- MENCHER, W. H., AND LEITER, H. E.: Anaerobic infections following operations on the urinary tract. *Surg. Gynec. & Obst.*, 66: 677, March 1938
- MERTZ, H. O., AND HAMER, H. G.: Urology in children. *Trans. Western Branch Am. Urol. Assoc.*, 6: 82, 1937
- MEYER, A. W.: Bronzephlegmone nach Nierenoperationen. *Arch. f. klin. Chir.*, 171: 39, 1932
- MINTZ, E. R.: Sarcoma of the kidney in adults. *Ann. Surg.*, 105: 521, 1937
- MINTZ, E. R.: Roentgen diagnosis in 94 cases of renal tumor. *J. Urol.*, 39: 244, 1938
- MITCHELL, A. G.: Nephrosclerosis (chronic interstitial nephritis) in childhood, with special reference to renal rickets. *Am. J. Dis. Child.*, 40: 101, and 345, 1930
- MYER, C. G.: Malignant tumors of the kidney in infancy and childhood. *Ann. Surg.*, 96: 1017, 1932

- MORRIS, H. L.: Demonstration and significance of nephroptosis and urinary stasis. *Radiol.*, 18: 56, 1932.
- MORRISSEY, J. H., AND SMITH, F. W.: Symptomatology and diagnosis of polycystic disease. *Med. J. & Rec.*, 199: 494, 1924.
- MOSETHAL, H. O.: Symposium of urologic disease and hypertension. *N. Y. State J. Med.*, 41: 953, 1941.
- MUNGER, A. D.: Acute hemorrhagic cyst of the kidney. *J. Urol.*, 27: 73, 1932.
- MURPHY, F. D. *et al.*: Lipoid nephrosis: a study of 9 patients with special reference to those observed over a long period. *Arch. Int. Med.*, 62: 355, 1938.
- MURPHY, F. D., AND PETERS, B. J.: Treatment of acute nephritis. *J. A. M. A.*, 118: 183, 1942.
- MURPHY, F. D., AND RASTETTER, J. W.: Acute glomerulonephritis, with special reference to the course and prognosis. *J. A. M. A.*, 111: 668, 1938.
- MUUS, N. R.: *Virchow's Arch. f. path. Anat.*, 155: 401, 1899.
- NECKER, F.: Parenchyma terungen der niere. *Kongr. internat. Gesellsch. f. urol.*, pp. 299-358, 1936.
- NECKER, F.: Pyelitis, pyelonephritis und pyonephrosis. *Handbuch d. Urol.*, (A. von Lichtenberg, *et al.*) 3: 690, 1928.
- NESBIT, R. M., AND DICK, D. S.: Acute staphylococcal infections of the kidney. *J. Urol.*, 43: 623, 1940.
- NESBIT, R. M., AND RATLIFF, R. K.: Hypertension associated with unilateral renal disease. *J. A. M. A.*, 116: 194, 1941.
- NESBIT, R. M., AND RATLIFF, R. K.: Hypertension associated with unilateral nephropathy. *J. Urol.*, 43: 427, 1940.
- NICHOLSON, G. W.: Embryonic tumor of the kidney in the fetus. *J. Path. and Bacteriol.*, 34: 711, 1931.
- OCKERBLAD, N. F., AND CARLSON, H. E.: Malignant papillary cystadenoma in a double kidney. *J. Urol.*, 40: 572, 1938.
- O'CONOR, V. J.: Carbuncle of the kidney. *J. Urol.*, 30: 1, 1933.
- O'CONOR, V. J.: Injuries to the kidney, with remarks on the effect of trauma, etc. *Industrial Med.*, 5: 268, 1936.
- OFFENHEIMER, G. D.: Polycystic disease of the kidney. *Ann. Surg.*, 100: 1136, 1934.
- OFFENHEIMER, G. D., AND POLLACK, H.: Attempted solution of renal calculi by dietetic measures. *J. A. M. A.*, 108: 349, 1937.
- OSBORNE, T. B., MENDEL, L. B., AND FERRY, E. L.: Phosphatic incidence of urinary calculi in rats fed on experimental rations. *J. A. M. A.*, 69: 32, 1917.
- OSMAN, A. A.: Studies in Bright's disease: the removal of septic foci in the upper respiratory tract in cases of unresolved acute nephritis. *Guy's Hosp. Repts.*, 83: 507, 1933.
- PAGE, J. M.: The diagnosis of renal tuberculosis. *Am. J. Surg.*, 56: 230, 1942.
- PAGE, I. H.: Production of arterial hypertension. *J. A. M. A.*, 113: 2046, 1939.
- PAGE, I. H.: On the nature of the pressor action of renin. *J. Exper. Med.*, 70: 521, 1939.
- PAGE, I. H.: Arterial hypertension. *J. Urol.*, 46: 807, 1941.
- PAGE, I. H.: Studies on the mechanism of arterial hypertension. *J. A. M. A.*, 120: 757, 1942.
- PAPIN, E.: Diagnostic de la tuberculose renale. *La Pratique Med.* III, Paris, G. Doin et Cie, 1931.
- PARK, W. H., AND WILLIAMS, A. W.: Pathogenic microorganisms, p. 564. Phila., Lea & Febiger, 1933.
- PATCH, F. S.: Typhoid infections of the kidney. *J. Urol.*, 14: 199, 1925.
- PATCH, F. S.: The association between leukoplakia and squamous-cell carcinoma in the upper urinary tract. *New England J. Med.*, 200: 423, 1929.

- PATCH, F. S., AND REID, R. G.: Carbuncle of the kidney with report of 2 cases of bilateral involvement. *Trans. Am. Assoc. Genito-Urin. Surg.*, 25: 1, 1932.
- PEACOCK, A. H.: Actinomycosis of the kidney. *Northwest. Med.*, 24: 173, 1925.
- PEACOCK, A. H., AND BALLE, A.: Renal lipomatosis. *Ann. Surg.*, 102: 395, 1936.
- POLKEY, HUGH: Xanthine calculi. *Urol. & Cutan. Rev.*, 38: 60, 1934.
- POTTS, W. J.: Squamous-cell carcinoma of the renal pelvis, associated with stone and leukoplakia. *Arch. Surg.*, 25: 458, 1932.
- POWERS, J. H., *et al.*: Juvenile hypertension associated with unilateral lesions of the upper urinary tract. *J. A. M. A.*, 118: 600, 1942.
- PRATHER, G. C.: Urological complications during pregnancy. *J. Indiana M. A.*, 30: 371, 1937.
- PRATHER, G. C.: Calyceal diverticulum. *J. Urol.*, 45: 55, 1941.
- PRATHER, G. C., AND CRABTREE, E. G.: Kidney tumors in children. *J. Urol.*, 25: 589, 1931.
- PRATHER, G. C., AND FRIEDMAN, H. F.: The immediate effect of preoperative radiation in cortical tumors of the kidney. *New England J. Med.*, 215: 15, 1936.
- PRATHER, G. C., AND SEWALL, W.: Recurrent pyelonephritis during pregnancy. *New Engl. M. J.*, 226: 291, 1942.
- PRICE, N. L., AND DAVIS, T. B.: Renal rickets. *Brit. J. Surg.*, 24: 548, 1937.
- PRIESTLEY, J. T.: Non-papillary squamous-cell epithelioma of the renal pelvis. *J. Urol.*, 37: 674, 1937.
- PRIESTLEY, J. T., AND BRODERS, A. C.: Wilms' tumor: clinical and pathologic study. *J. Urol.*, 33: 544, 1935.
- PRIESTLEY, J. T., AND BRODERS, A. C.: Wilms' tumor: most common malignant growth affecting children. *Proc. Staff Mtg. Mayo Clinic*, 10: 81, 1935.
- PRIESTLEY, J. T., AND PILCHER, F., JR.: Traumatic lesions of the kidney. *Am. J. Surg.*, 40: 357, 1938.
- QUINBY, W. C.: Factors influencing the operative procedure in hydronephrosis. *J. A. M. A.*, 93: 1709, 1929.
- QUINBY, W. C., AND BRIGHT, E. F.: Solitary renal cysts; symptoms when situated at upper pole of right kidney. *J. Urol.*, 33: 201, 1935.
- RANDALL, ALEXANDER: Prevention of the recurrence of urinary calculus. *Am. J. Surg.*, 18: 482, 1932.
- RANDALL, ALEXANDER: Origin and growth of renal calculi. *Ann. Surg.*, 105: 1009, 1937.
- RANDALL, ALEXANDER: The etiology of primary renal calculus. *Repts. VII Congress Int. Soc. Urol.*, 1939. *Surg., Gynec. & Obst. (Int. Abst. Surg.)*, 71: 209, 1940.
- RANDALL, ALEXANDER: Papillary pathology as a precursor of primary renal calculus. *J. Urol.*, 44: 580, 1940.
- RANDALL, ALEXANDER, AND MELVIN, P. D.: The morphogeny of renal calculus. *Trans. West. Branch Am. Urol. Assoc.*, 3: 1, 1936.
- RATHBUN, N. P.: Resection of the kidney: report of 6 cases. *Am. J. Surg.*, 13: 565, 1931.
- RAVICH, A.: Multilocular tuberculous cyst of the kidney, complicated by calculus. *Urol. & Cutan. Rev.*, 43: 319, 1939.
- RAVICH, A., AND TURKELTAUB, S. M.: Solitary cysts of the kidney. *Urol. & Cutan. Rev.*, 41: 261, 1937.
- REAVES, ULLMAN: (Discussion of LeComte's paper, 1938).
- REDMAN, J. L., AGERTY, H. A., BARTHMAIER, O. F., AND FISHER, H. R.: Neuroblastoma; report of case and review of literature. *Am. J. Dis. Child.*, 56: 1097, November 1938.
- REIMANN, H. A.: Typhoid pyelonephritis; renal typhoid fever. *J. A. M. A.*, 111: 691, 1938.
- RICH, A. R., AND MCCORDOCK, H. A.: The pathogenesis of tuberculous meningitis. *Bull. Johns Hopkins Hosp.*, 52: 5, 1933.

- RIMBAUD, P.: Cortical tumors and disorders of arterial tension. *Progres. med.*, 67: 857, June 17, 1939.
- ROBERTSON, J. P.: Injuries of the kidney. *Southern M. J.*, 35: 181, 1942.
- ROBINSON, L. J., AND WILDER, W. O.: Simple solitary renal cyst. *J. Urol.*, 40: 10, 1938.
- ROLNICK, H. C.: Injuries to the kidney. *Illinois Med. J.*, 77: 77, 1931.
- ROLNICK, H. C.: Surgery in polycystic disease of the kidney. *J. Urol.*, 47: 648, 1942.
- ROLNICK, H. C., AND BURNSTEIN, H. J.: Perinephritic abscess. *J. Urol.*, 25: 507, 1931.
- ROSE, D. K., *et al*: Kidney pelves, normal variations in their shape and flow, with possible pathological significance. *Surg. Gynec. & Obst.*, 57: 1, 1933.
- ROSE, D. K., AND ROLLINS, P. R.: Pyelonephritis in pregnancy; its treatment and prevention based on cystometric conclusions. *J. A. M. A.*, 96: 235, 1931.
- ROSENOW, E. C.: Results on experimental studies on focal infection and elective localization. *Med. Clin. North Am.*, 5: 573, 1921.
- ROSENOW, E. C., JR.: Renal calculi—a study of papillary calcification. *J. Urol.*, 44: 19, 1940.
- ROSENOW, E. C., AND MEISSER, J. G.: The production of urinary calculi by the devitalization and infection of teeth in dogs with streptococci from cases of nephrolithiasis. *Arch. Internat. Med.*, 31: 807, 1923.
- ROTH, L. J., AND DAVIDSON, H. B.: Fibrosis and fatty replacement of the renal parenchyma. *J. A. M. A.*, 111: 233, 1938.
- ROWNTREE, L. G.: Hypertension and unilateral disease of the kidney. *Urol. & Cutan. Rev.*, 44: 24, 1940.
- RUBIN, M. I., AND RAPOPORT, M.: Cardiac complications of acute hemorrhagic nephritis. *Am. J. Dis. Child.*, 55: 244, 1938.
- SANFORD, A. H., AND VOELKTR, M.: Actinomycosis in the United States. *Arch. Surg.*, 11: 809, 1925.
- SCHARTZ, JOSEPH: Unilateral multicystic kidney in an infant. *J. Urol.*, 35: 259, 1936.
- SCHENCK, G. F.: Traumatic rupture of the kidney. *Calif. & West. Med.*, 40: 341, 1934.
- SCHOLL, A. J.: Tumors of the adrenal cortex. *J. Urol.*, 39: 81, 1938.
- SCHOLL, A. J.: Hemorrhagic cysts of the kidney: case. *J. Urol.*, 41: 103, February 1939.
- SCHROEDER, H. A.: Essential hypertension. *Am. J. Med. Sci.*, 204: 734, 1942.
- SCHROEDER, H. A., AND FISH, G. W.: Studies on essential hypertension. III. Effect of nephrectomy upon hypertension associated with organic renal disease. *Am. J. Med. Sci.*, 199: 601, 1940.
- SCHROEDER, H. A., AND STEELE, J. M.: Abnormalities in the urinary tract in "essential hypertension." *Proc. Soc. Exper. Biol. & Med.*, 39: 107, 1938.
- SCHROEDER, H. A., AND STEELE, J. M.: Studies on "essential" hypertension: I. Classification. *Arch. Int. Med.*, 64: 927, 1939.
- SCHUMACKER, PAUL: Ergebnisse der intravenösen pyelographie und röntgenologischen suffizienzprüfung der vesicalen ureterostien bei der pyelitis gravidarum. *Arch. f. Gynak.*, 147: 662, 1931.
- SCOTT, DOUGLAS E.: The effects of pressure of pyelographic media. *J. Urol.*, 30: 39, 1933.
- SCOTT, W. W.: Blood-stream infections in urology: report of 82 cases. *J. Urol.*, 21: 527, 1929.
- SENGER, F. L., AND BOITONE, J. J.: Primary epithelial tumors of the renal pelvis. *Am. J. Surg.*, 37: 57, 1937.
- SHAEFFER, A. J., AND REMSEN, D.: The relation of urinary infection to chronic nephritis in childhood. *Acta Paediat.*, 22: 415, 1938.
- SHAPIRO, I. J., AND VISEEN, L.: Untoward results in bilateral pyelography. *J. Urol.*, 24: 621, 1930.
- SHAW, E. C.: Advantages and dangers of indwelling ureteral catheter in kidney infections. *Southern M. J.*, 21: 899, 1928.

- SHELLING, D. H., AND REMSEN, D.: Renal rickets. *Bull Johns Hopkins Hosp.*, 57: 158, 1935.
- SHIVERS, C. H. DET.: A possible mistake in the diagnosis of gonococcal infection of the kidney. *J. A. M. A.*, 80: 1359, 1923.
- SIMMONS, R. R.: Gonococcal infections of the kidney. Report of a case with traumatic rupture. *J. Urol*, 7: 113, 1922.
- SIMON, JULES Contribution à l'études des grandes kystes sereux du rein. Paris Thésis, 1906
- SMITH, G. G.: Renal infection due to dilatation of single calyx. *Trans Am Assoc Genito-Urin. Surgeons*, 26: 307, 1933
- SMITH, H. W.: Studies on the physiology of the kidney; renal blood flow in normal and hypertensive subjects. *Univ. Kansas*, 1939
- SOUTHAM, A. H.: Fixation of the kidney. *Quart J. Med*, 16: 283, 1923
- SPITZER, W., AND HILLKOWITZ, P.: The cause of stone in the urinary tract. *J Urol*, 11: 327, 1924
- SPOONER, L. H.: The bacteriology of tuberculous kidneys. *J. Med. Research*, 39: 59, 1918.
- STANTON, E. M.: Actinomycosis limited to the urinary tract. *Am Med*, 11: 401, 1906
- STEDMAN, HAROLD E.: Carbuncle of the kidney: report of 2 cases. *Am J Surg.*, 42: 410, 1938
- STEINER, MORRIS, ZUGER, B., AND KRAMER, B.: Production of renal calculi in guinea pigs by feeding them a diet deficient in vitamin A. *Arch Path* 27: 104, 1939.
- STERN, R. O., AND NEWNS, G. H.: Wilms' embryoma; clinico-pathological study. *Arch Dis Childhood*. 13: 193, September 1938
- STEVENS, A. R.: Schistosomiasis involvement of the upper urinary tract. Report of patient with papillomata of the renal pelvis, ureter, and later of the bladder. *Trans Am Assoc Genito-Urin Surg*, 28: 275, 1935
- STEVENS, W. E.: Roentgenologic examination of the kidney with special reference to back-flow and injuries associated with retrograde pyelography. *Trans Am Assoc Genito-Urin. Surg*, pp 169-182, 1937.
- STIRLING, W. C.: Large solitary hemorrhagic renal cyst; review of literature. *J. Urol*, 25: 213, 1931.
- STIRLING, W. C., AND ASH, J. E.: Papillary adenocarcinoma of the kidney. *Surg, Gynec. & Obst.*, 73: 305, 1941.
- STIRLING, W. C., AND LANDS, A. M.: Experimental study of kidney trauma. *J. Urol*, 37: 466, 1937. See also: *J d'urol*, 43: 307, 1937, and *Brit. J. Urol*, 8: 1, 1936
- STOBBAERTS, F.: Suites medico-legales des traumatismes des reins. *Jour belge d'urol*, 10: 89, 1937.
- SUCKLING, C. W.: Nephroptosis, dropped kidney, its effect upon the nervous system, with special reference to insanity. *Lancet. Clinic*, 304: 331, 354, 1913.
- SURRACO, L. A.: The pyelographic diagnosis of polycystic kidneys. *Rev. Med Latino-Americana*, 290: 144, 1939 (Abstr. *Brit. J. Urol*, 12: 140, 1940)
- TAYLOR, W. N.: Leukoplakia of the kidney pelvis and ureter. *Am. J. Surg.*, 32: 335, 1936.
- THOMAS, B. A., AND HARRISON, F. G.: Clinical pathology of nephroptosis; is prevalent conception of treatment correct? (Discussion by H. L. Morris and C. M. McKenna). *Trans. Sec. Urol*, A. M. A., p. 242, 1938.
- THOMAS, G. J.: Renal tuberculosis. *J. A. M. A.*, 94: 229, 1930.
- THOMAS, G. J. *et al*: Surgical treatment of urogenital tuberculosis. *J. Urol*, 39: 766, 1938.
- THOMAS, G. J., AND KINSELLA, T. J.: Renal tuberculosis; preliminary report of a clinical research problem. *J Urol*, 17: 395, 1927.
- THOMAS, G. J., AND KINSELLA, T. J.: Modern concepts of genito-urinary tuberculosis. *Am I. Surg.*, 23: 111, 1934

- THOMAS, G. J., STEBBINS, T. L., AND PETTER, C. K.: The diagnosis and indications for treatment of renal tuberculosis. *Am. J. Surg.*, 38: 57, 1937.
- THOMAS, G. J., STEBBINS, T. L., AND SANDELL, S. T.: Control and arrest of lesions of renal tuberculosis. *J. Urol.*, 46: 579, 1941.
- THOMPSON, C. J., AND BUMPUS, H. C.: Ureteral kinks. *J. A. M. A.*, 94: 771, 1930.
- TRAUT, H. F., *et al.*: Physiologic changes in the ureter associated with pregnancy, etc. *Surg. Gynec. & Obst.*, 64: 51, 1937.
- TURNER, B. W.: Gas bacillus infection of the urinary tract: report of 2 cases following kidney operations. *Urol. & Cutan. Rev.*, 38: 153, 1934.
- TURNER, J. H.: Tuberculous meningitis following nephrectomy. *J. Urol.*, 34: 216, 1935.
- TWINEM, F. P.: Polycystic kidneys, with bilateral perinephritic abscesses: bilateral operation: case. *J. A. M. A.*, 106: 206, 1936.
- TWINEM, F. P.: A study of recurrence following operations for nephrolithiasis. *J. Urol.*, 37: 259, 1937.
- TWINEM, F. P.: Prevention of recurrent renal stone by calyceal resection. *Surg. Clin. North Am.*, 20: 299, 1940.
- TWINEM, F. P.: Relation of renal stone formation and recurrence to calyceal pathology. *J. Urol.*, 44: 596, 1940.
- UFFEDEDUZZI: Bilateral tuberculosis of the kidney; clinical and experimental study. *Arch. d. mal. d. reins*, 9: 574, 1935.
- UHLE, C. A. W.: The significance of aneurysm of the abdominal aorta masquerading as primary urologic disease. *J. Urol.*, 45: 13, 1941.
- VAN LEERSUM, E. C.: Vitamin A deficiency and urolithiasis. *J. Biol. Chem.*, 76: 137, 1928.
- VAN DER VUURST DE VRIES, J. H. J.: De l'utilité ou de la nécessité des explorations successives chez les malades chez lesquels on a constaté à un moment donné une tuberculose rénale bilatérale. *J. d'urolog.*, 46: 526, 1938.
- VERMOOTEN, V.: The mechanism of perinephric and perinephritic abscess. *J. Urol.*, 30: 181, 1933.
- VERMOOTEN, V., AND McKEOWN, R. M.: Renocolic fistulae. *Am. J. Surg.*, 21: 242, 1933.
- VERRIERE, P.: Un cas de traumatisme grave du rein étudié et surveillé par pyelographies successives. *Bull. Soc. franç. d'urolog.*, p. 220, May 18, 1936.
- VIRCHOW, R.: Discussion of Ewald's presentation: Zur totalen cystischen degeneration der nieren. *Deutsch. Med. Wchnschr.*, 18: 36, 1892.
- VON LICHTENBERG, A.: Primäre nierenaktinomykose. *Handbuch d. Urol.*, 4: p. 225. Berlin, Springer, 1929.
- WALLACE, CUTHBERT: A study of 1200 cases of gunshot wounds of the abdomen. *Brit. J. Surg.*, 4: 679, 1916-17.
- WALKER, R. M.: Spontaneous rupture of hydronephrosis. *Brit. J. Urol.*, 5: 139, 1933.
- WALTERS, W., AND KEPLER, L. J.: Cortical tumors and their treatment; 7 operated cases. *Ann. Surg.*, 107: 881, June 1938.
- WANG, S. L.: The medical aspects of urologic tuberculosis. *Long Island M. J.*, 22: No. 5, 1928.
- WANG, S. L.: Tuberculin therapy in urologic tuberculosis. *J. A. M. A.*, 94: 235, 1930.
- WANG, S. L.: Factors in the treatment of postoperative and inoperable tuberculosis of the genito-urinary tract. *Am. J. Surg.*, 11: 88, 1931. Also: *Am. Rev. Tuberculosis*, 28: No. 6, December 1933.
- WANG, S. L.: Quartz light therapy in urogenital tuberculosis. *J. A. M. A.*, 104: 720, 1935.
- WANG, S. L.: Medical care in the treatment of urogenital tuberculosis. *Urol. & Cutan. Rev.*, 46: 696, 1942.
- WATKINS, K. H.: Cysts of kidney due to hydrocalycosis. *Brit. J. Urol.*, 11: 245, 1939.

- WEBSTER, R.: Pathological reports from the Children's Hospital, Melbourne: Renal tuberculosis in childhood. *Med. J. Australia*, 1: 21, January 7, 1939.
- WEBSTER, R.: Pathological reports from Children's Hospital, Melbourne; Neuroblastoma. *M. J. Australia*, 26, No 1: 193, February 4, 1939.
- WEISS, S., AND PARKER, F.: Relation of pyelonephritis and other urinary tract infections to arterial hypertension. *New Engl. M. J.*, 223: 9591, 1940.
- WELLS, C.: Polycystic and "unilateral" polycystic kidneys; review of literature and report of 2 cases, one with intracystic papilloma. *Brit. J. Urol.*, 8: 22, 1936.
- WESSON, M. B.: Renal calculi. etiology and prophylaxis. *J. Urol.*, 34: 289, 1935.
- WESSON, M. B., AND FULMER, C. C.: Aneurysm of the renal artery. *Am. J. Roentgenol.*, 33: 176, 1935.
- WHARTON, L. R.: Preoperative irradiation of massive tumors of the kidney. *Arch. Surg.*, 30: 35, 1935.
- WHARTON, L. R. *et al*: The late effects of acute pyelitis in girls. *J. A. M. A.*, 119: 1597, 1937.
- WILDBOLZ, HANS: Experimentale studien ueber aszendierende nierentuberkulose. *Folia. urologica*, 3: 6, 1909.
- WILDBOLZ, HANS: Experimentell erzeugte aszendierende nierentuberkulose. I. Kongr. d. Deutsch. Gesellsch. f. Urol., 1907.
- WILDBOLZ, HANS: Ueber der moeglichkeit einer spontanheilung der nierentuberkulose. *Ztschr. f. urol Chir u. Gynak.*, 42: 257, 1936.
- WILDBOLZ, HANS: Ueber die behandlung der genitaltuberkulose des mannes. *Ztschr. f. urol.*, 30: 7, 1936.
- WILLIAMS, H. U.: *Bacillus aerogenes capsulatus* in suppurative pyelitis. *Johns Hopkins Hosp Bull.*, 7: 66, 1896.
- WILLIAMS, J. R., JR., HARRISON, T. R., AND MASON, M. F.: Observations on two different pressor substances from extracts of renal tissue. *Am. J. Med. Sci.*, 195: 339, 1938.
- WILMS, M.: Die mischgeschwuelste, 1: 1-90 Leipzig, A. Georgi, 1899.
- WINSBURY-WHITE, H. P.: The radiographic features of urinary calculi in relation to their chemical composition and structure, with special reference to renal calculi. *Brit. J. Surg.*, 12: 5, 1924.
- WINSBURY-WHITE, H. P.: Leukoplakia in the urinary tract: case. *Brit. J. Surg.*, 20: 49, 1932.
- WINSBURY-WHITE, H. P.: The spread of infection from the uterine cervix to the urinary tract, and ascent of infection from the lower urinary tract to the kidneys. *Brit. J. Urol.*, 5: 249, 1933.
- WOLBACH, S. B.: The pathologic changes resulting from vitamin deficiency. *J. A. M. A.*, 108: 7, 1937.
- WOOD, A. H.: Diagnosis and treatment of kidney trauma. *J. Urol.*, 37: 437, 1937.
- WOODRUFF, S. R.: The traumatized kidney; a study of the after-effects. *J. Med. Soc. New Jersey* 27: 208, 1930.
- WOODRUFF, S. R., AND BUMPUS, H. C., JR.: Is nephrectomy always indicated following a diagnosis of unilateral renal tuberculosis? *J. A. M. A.*, 104: 716, 1935.
- WOODRUFF, S. R., AND GROSSMAN, S. L.: Renal carbuncle: case. *Urol. & Cutan. Rev.*, 40: 240, 1936.
- WOODRUFF, S. R., AND MILBERT, A. H.: Roentgenographic studies of the urinary tract during and after pregnancy. *J. A. M. A.*, 3: 1607, 1938.
- WOODRUFF, S. R., AND SHERER, ROLAND: Renal ptosis. *J. Urol.*, 35: 125, 1936.
- WRIGHT, J. H.: Neurocytoma or neuroblastoma, a kind of tumor not generally recognized. *J. Exper. Med.*, 12: 556, 1910.

- YOUNG, H. H.: Practice of urology, Vol. I, p 746. Phila, W. B. Saunders Co., 1926.
- YOUNG, H. H.: Lipomatosis or destructive fat replacement of the renal cortex. J. Urol, 29: 631, 1933.
- YOUNG, H. H.: Genital abnormalities, hermaphroditism, and related adrenal diseases Baltimore, Williams & Wilkins Co., 1937.
- YOUNG, H. H., AND WATERS, C. A.: Urological roentgenology. Chapt. V, pp 245, 253. N. Y., P. B. Hoeber, 1929.
- ZIMMERMAN H. B.: Localized actinomycosis Minnesota Med., 14: 759, 1931.





CHAPTER XXXVIII

OPERATIVE AND NON-OPERATIVE TREATMENT OF THE KIDNEY

A. OPERATIVE TREATMENT OF THE KIDNEY

Importance of Preliminary Examination

If the diagnosis has been made in accordance with modern methods, the general condition of the patient coming for renal surgery will have been thoroughly investigated, and a detailed report as to the exact state of his urinary tract will be at hand.

Before undertaking any intervention upon a kidney, it is essential to know the precise status of the one that is not to be operated upon. It is not enough to know that the opposite kidney is present and functioning; it must also be determined whether or not there exist any anomalies of the upper urinary tract, or other factors, which may upset the surgeon's calculations. Except in emergencies, such as renal injuries resulting from accidents, this careful preliminary survey should never be omitted. Should it be necessary to remove a badly injured or diseased kidney without such previous examination, the surgeon will be obliged, after exposure of the supposedly sound kidney, to explore it with his hand in order to ascertain whether or not its functional ability is sufficient to sustain life in the event that nephrectomy is done. This is not so difficult if the procedure is intra-abdominal; but in extraperitoneal operations it is necessary to incise the peritoneum at the side of the kidney undergoing operation so that the surgeon may make an investigation through this opening.

Anesthesia

In no branch of surgery is the anesthetic of greater importance than in operations upon the kidneys. Our personal experience, which has embraced all the recognized methods of producing anesthesia, leads us to believe that for interventions upon the kidney some form of regional anesthesia is usually preferable to any type of general anesthesia. In our clinic, most renal operations are now done under spinal anesthesia. For

a number of years we employed paravertebral anesthesia almost exclusively for operations upon the kidney, and still consider this a useful method; but improved drugs and technic have so increased the safety and efficacy of spinal anesthesia that, in common with most urologists, we now regard this as the method of choice in renal surgery.

We do not, however, advocate that regional anesthesia be employed routinely, for there are patients whose temperament makes it impossible to carry out even a minor procedure while they are conscious of what is going on. Unless the cooperation of the patient can be obtained, regional anesthesia is quite out of the question. Usually the attainment of this cooperation is not difficult. However, for children and highly nervous patients general inhalation anesthesia is advisable.

Regional anesthesia is especially indicated in cases complicated by cardiac lesions, advanced arteriosclerosis, or any form of pulmonary disease—tuberculosis in particular. In bilateral renal disease, ether anesthesia is particularly to be avoided, as a crippled kidney may have to assume the work of both sides while its mate undergoes operation, and the added strain of ether anesthesia, with its well-known irritative effect upon renal tissue, may bring about a rapidly fatal termination.

The various methods of producing anesthesia are described in detail under Anesthesia in Urology (Chapter VI).

Preoperative Preparation

General Preparation of Patient. The patient is prepared in the usual manner in regard to catharsis and enemas. A soapsuds enema is given the evening before the operation and again the following morning.

Fluids should be taken freely up to the time of operation, and, if regional anesthesia is to be used, the patient is permitted a light breakfast. When general inhalation anesthesia is selected, breakfast and fluids are, of course, withheld.

Preoperative Narcosis. At bedtime, the evening before the operation, the patient is given analgesic medication by mouth. We have found phenobarbital or nembutal, 0.1 Gm. very satisfactory for this purpose. The patient is again given phenobarbital or nembutal, 0.2 Gm. one hour before going to the operating room (Preliminary Medication, p. 191).

Preparation of the Skin

In our service, the skin is cleansed with green soap and warm water, and sterilized with alcohol and tincture of zephiran 1:1,000 or tincture of merthiolate. 1:1,000. The entire field of operation must be sterilized—

that is, from the breast-bone to the buttock, the side limits being the umbilicus in front and beyond the vertebral column behind.

Position of Patient on Operating-Table

For transperitoneal incision, the position of the patient on the operating-table, and the surgeon's place, are the same as for operation upon the median abdominal region.

For the extraperitoneal lumbar incision, the patient is placed on the table on the side opposite that to be operated upon, with the lower border of the ribs over the elevator. If there is no elevator on the table, a sand-bag or cushion is placed under the back directly below the position of the last rib. This forces the side to be operated upon upward, increasing the space between the iliac crest and the last rib. The patient's upper arm is flexed in front of the face. The lower arm is drawn back, allowing it to lie flat. Care must be taken that the fingers are so placed as not to become caught in the mechanism of the table when the elevator is raised or lowered. The under leg is flexed at right angles, as close to the body as possible. The upper leg is extended. The elevator is then raised. A knee-strap is adjusted above the knee of the extended leg. Care must be taken to pad all places where the braces come in contact with the body.

A wide strip of adhesive tape is useful for fixing the patient in position; this is fastened across the hips and attached to the edges of the table. Many types of mechanical apparatus have been suggested for holding the patient firmly in the desired position—a most important factor in renal surgery—but we have found the proper application of adhesive straps the simplest and best method of all.

The surgeon takes up his position at the patient's back, with his assistant opposite.

Incisions Employed in Renal Surgery

There are two major routes of access to the kidney: (1) the lumbar incision, which leaves the peritoneum intact; (2) abdominal laparotomy, which is, of course, transperitoneal. The lumbar incision is the one most commonly used. In some cases it is necessary to approach the kidney from two directions, a procedure which may be said to constitute a third method.

Anatomical Landmarks. Before making any incision, the operator should make sure of his position by locating all the essential anatomical

landmarks. The ribs should be counted from above downward, for many persons are without a twelfth rib, and many others have a thirteenth rib. If it is merely assumed that the twelfth rib is present, incision may invade the pleura, should the rib actually be absent; and if the patient possesses a thirteenth rib, an incision carried only to the twelfth rib would give too contracted an opening. The tips of the eleventh and twelfth ribs should be found and indicated, and the location of the crest of the ilium, the anterior-superior spine of the ilium, and the anterior edge of the erector spinous process definitely established.

Extraperitoneal Lumbar Exposure. The ordinary route of access to the kidney is by the lumbar incision, cutting through the muscles filling the space below the twelfth rib, opening Gerota's capsule, but leaving the peritoneum intact. The incisions used in operations under regional anesthesia must be larger than those ordinarily used when the patient is given general anesthesia. This is necessary in order to avoid heavy retraction, which is always painful.

The customary incision extends parallel with the twelfth rib and about 2 cm. below it, from the costovertebral angle downward and forward to a point about 3 cm. above the crest of the ilium. Should a larger opening be necessary, the incision can be extended forward toward the abdomen, or it may be curved downward on a line with the iliac crest, terminating directly over the anterior-superior spine of the ilium.

The initial incision is carried down through the skin, superficial fascia, deep fascia, the external oblique, internal oblique, and transversus abdominis muscles, and the transversalis fascia, the peritoneum being dissected away from the abdominal wall by blunt dissection. The twelfth nerve is isolated and retracted at the posterior angle of the wound. All bleeding points are clamped and ligated. The perirenal fascia (Gerota's capsule) is then opened at the posterior angle of the wound, and the opening enlarged by blunt dissection, exposing the kidney. The kidney is dissected free from the surrounding adipose tissue by sharp and blunt dissection. If branches of the ilio-hypogastric and ilio-inguinal nerves appear during the dissection of the fatty tissue, they should be carefully avoided.

The likelihood of encountering aberrant blood vessels must constantly be kept in mind. The poles of the kidney should be freed very cautiously and the organ gradually mobilized, the tissues being carefully inspected before they are severed. The surgeon should also be alert to detect the pulsation of a possible anomalous artery.

Delivery of the Kidney. When the kidney has been freed from its fatty capsule, and all vessels likely to produce embarrassing hemorrhage have been properly ligated, the organ may be lifted up into the wound for inspection and whatever operative procedure it is proposed to apply to it. There must be absolute assurance that the entire surface of the kidney has been freed up to the pedicle, and, in lifting it, great care must be exercised not to bring too much traction to bear upon the pedicle, as damage to the important blood vessels contained in this structure may have immediately fatal results.

Before attempting to mobilize the kidney, it is well to locate the ureter, which usually can be done by retracting the peritoneal covering and palpating it with the fingers. When pyelotomy is to be done, the ureter may be isolated and a tape passed beneath it to facilitate its manipulation.

Accidents to be Guarded Against. Accidents to be guarded against, in making this incision, are wounding of the peritoneum and cutting into the pleura. Should the peritoneum be accidentally injured, it must be quickly repaired by sutures. The last rib, when normally placed, usually acts as an efficient shield for the pleura, so that accidental incision probably takes place only when this rib is misplaced or congenitally shortened.

Abdominal Incision. It is because the surgeon must enter the peritoneal cavity, if he makes his incision through the abdominal wall, that the lumbar operation is more generally done. The abdominal incision is usually made either through the median line or through the outer border of the rectus muscle on whichever side the affected kidney is located. On the left side, when the peritoneum has been opened the kidney can usually be easily made out to the inner side of the descending portion of the colon. On the right side, it will be more difficult to feel the kidney, as it is concealed behind the cecum and colon; but, unless adhesions are present, a hand passed beneath the liver at the outer side of the gall-bladder will usually encounter it.

Ectopic kidneys must, of course, be approached by the transperitoneal route.

Nephrectomy

Excision of the kidney is necessary when there is destruction of the organ by disease or trauma, when there is partial destruction by tumor, or when a virulent infection, such as carbuncle, is present. It is most commonly accomplished through a lumbar incision, though the nature

of the condition which necessitates nephrectomy will naturally influence the method of approach.



FIG. 331. Extraperitoneal lumbar approach. (a) Skin incision extending parallel with the twelfth rib and above the crest of the ilium. (b) Showing Petit's triangle. (c) External and internal oblique muscle. (d) Internal oblique muscle. (e) Internal oblique muscle. (f) Internal oblique muscle. (g) Dividing the costovertebral ligament.

Extraperitoneal Lumbar Nephrectomy. The incision for the removal of a kidney usually extends parallel with the twelfth rib and about 2 cm. below it, from the costovertebral angle downward for a distance of about 15 cm. to a point just above the crest of the ilium (*Incisions Employed in Renal Surgery*, p. 1657).

The incision is deepened through the fasciae and the muscles filling the space below the twelfth rib, the peritoneum being dissected away from the abdominal wall by blunt dissection. Gerota's capsule is opened, exposing the kidney.

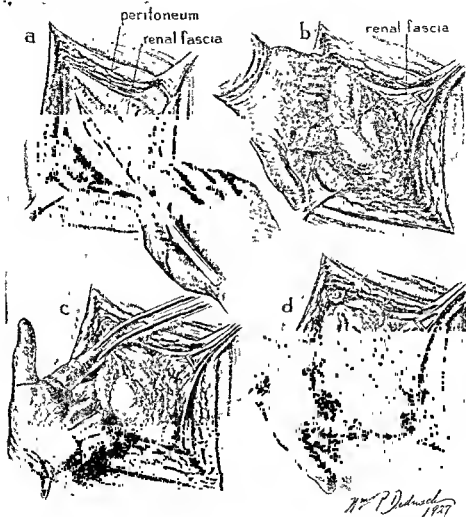
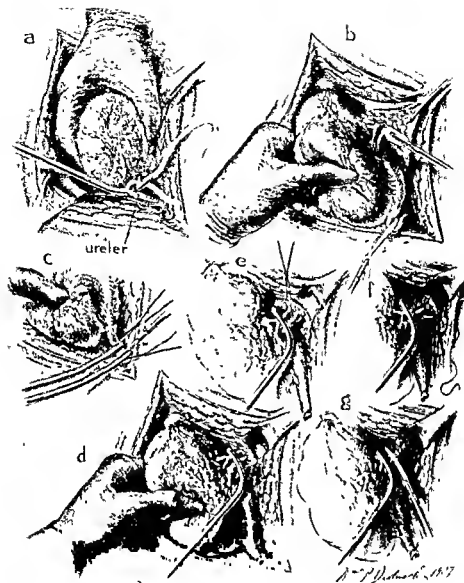


FIG. 272. Nephropathy of the kidney. (a) Incision of the renal fascia. (c) Exposure of the kidney.

After the kidney has been exposed, it must be freed from the tissues surrounding it, and the ease with which this is accomplished will depend upon the presence and number of adhesions, as well as upon the nature of



the disease affecting it. Adhesions should be divided with scissors, and every care taken to avoid hemorrhage before the vessels can be exposed and ligated. The kidney is freed on all sides until the pedicle is reached,

the pelvis and its ureter then being separated from the blood vessels and the ureter divided between two ligatures as far down as it can be reached. Both ends of the ureter are treated with carbolic acid, followed by alcohol.

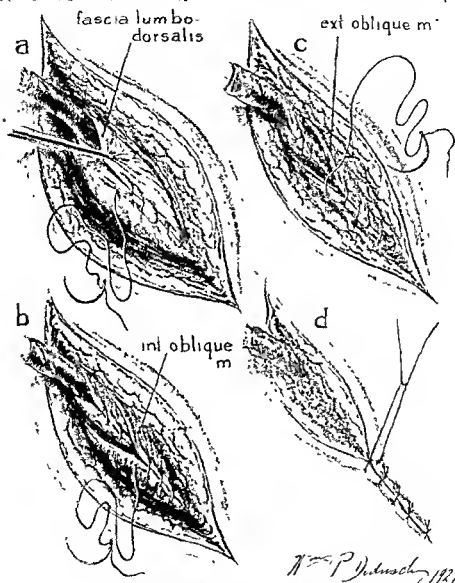


FIG. 334. Extraperitoneal lumbar nephrectomy. (a) Suturing the lumbodorsalis fascia; drain in place (b, c) Suturing the internal and external oblique muscles. (d) Suturing the skin.

Handling of the Vascular Pedicle. Having isolated the kidney and excised the ureter, the dissection is carried as close to the vascular

pedicle as possible under the existing pathological conditions. A renal-pedicle clamp is then applied. A double ligature of No. 2 chromic catgut, about 18 inches long, is carried around the pedicle below the clamp. A single knot is tied, the clamp being loosened as the knot is drawn tight; it is then retightened and the square knot completed. The kidney is cut free above the pedicle clamp, leaving a rosette of tissue above the knot of a size sufficient to prevent its retraction through the knot. A second knot may be similarly applied if it is deemed advisable. A double No. 2 chromic catgut transfixion suture is then applied beneath the pedicle clamp and tied as the clamp is removed. All small bleeding points are clamped and ligated.

By loosening the clamp as the knot is drawn tight, the ribbon-like clamped pedicle becomes tubular; and when the kidney is excised, leaving a rosette of tissue, it will not retract.

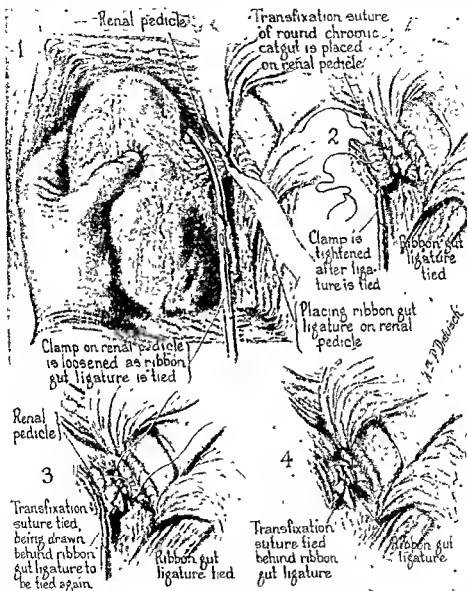
If the kidney pedicle has been subject to long-standing disease, such as tuberculosis, it is sometimes wise to tie it off with a piece of chromic ribbon gut, properly moistened, so that the ligature will not cut through the diseased vessels (Fig. 335).

Closure. A Penrose drain is placed in the wound. The transversalis fascia and transversus abdominis muscle are repaired with a continuous suture of No. 2 chromic catgut, the internal and external oblique muscles with interrupted sutures of No. 2 chromic catgut, the deep fascia with a continuous suture of No. 2 chromic catgut, and the superficial fascia and skin with interrupted black silk Stewart sutures.

Subcapsular Nephrectomy. In some cases of extensively diseased kidneys, or organs that have been much operated upon, the presence of many adhesions makes subcapsular nephrectomy necessary or desirable. This is easily accomplished without damage to the surrounding structures, and, by cutting through certain portions of thickened capsule, it is usually possible to dissect enough of it away to isolate the vascular pedicle sufficiently to tie it off.

Sometimes, however, the surgeon does not have the opportunity to isolate, clamp, and tie off the vascular pedicle properly. In such cases, it may be necessary to leave a clamp on the kidney pedicle. When this is done, it is our practice to tie a piece of catgut through the handles of the clamp, to impress upon everyone the importance of not removing the clamp. A helpful nurse once removed a clamp from the kidney pedicle 8 hours after nephrectomy, and the strange and wonderful thing is that nothing happened. Ordinarily, such a clamp is left on for a period

of 3 to 5 days; then, on the next day, it is loosened, a notch at a time, until entirely loose, being left in position so that, if bleeding occurs, it



may be stopped merely by retightening the clamp. On the fifth to seventh day it is removed.

Nephrectomy for Tuberculosis. A tuberculous kidney is frequently surrounded by dense adhesions and structurally weakened by cavities and pus pockets, making its removal difficult. The incision which we find most useful is a wide one, extending from the costovertebral angle outward and downward about 2 cm. below the lower edge of the twelfth

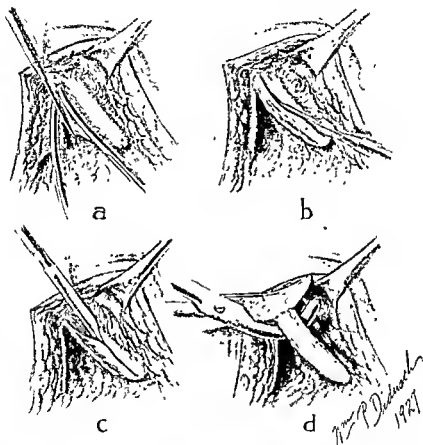


FIG. 336 *Resection of twelfth rib.* In performing nephrectomy it is occasionally necessary to resect the twelfth rib (a) Dividing the costovertebral ligament. (b) Incising the periosteum (c) Scraping or removing the periosteum from the bone (d) Resecting the rib

rib and to a point just above the anterior-superior spine of the ilium. If the pedicle is friable, we prefer to tie it off with plain ribbon gut, which will not cut through the diseased vessels.

Operative management of the tuberculous ureter is of the greatest importance. As infection of the ureteral stump often accounts for the persistence of urinary tuberculosis after nephrectomy, the grossly infected

ureter should be removed *in toto* down to the bladder whenever possible. In case the patient's condition does not make this extensive procedure advisable at the time of the nephrectomy, it may be necessary to do a

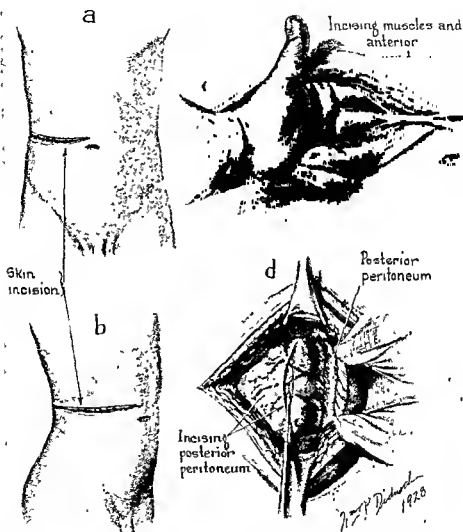


FIG 337. Transperitoneal nephrectomy for renal tumor. (a, b) Showing the skin incision. (c) Incising the muscles and anterior peritoneum (d) Incising the posterior peritoneum.

secondary operation for its removal at a later date. Temporizing with a grossly infected ureteral stump is rarely of any avail.

Another method of treating the tuberculous ureter has been utilized

by us of late. The ureter is cut off close to the renal pelvis and transplanted into the lower angle of the wound. This prevents any overflow of pus into the wound, all discharges pouring out into the dressings.

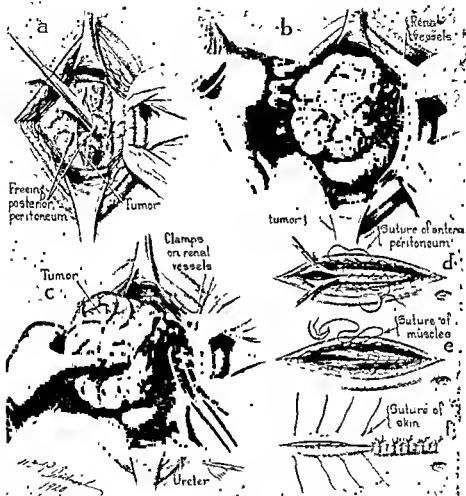


FIG. 338. Transperitoneal nephrectomy for renal tumor. (a) Freeing the posterior peritoneum. (b) Freeing the tumor mass. (c) Removing the kidney with the tumor. (d) Suture of anterior peritoneum. (e, f) Suturing muscles with chromic catgut No. 2, and skin with silk.

Transperitoneal Nephrectomy. Transperitoneal nephrectomy is rarely necessary, since, if one makes a sufficiently large incision in the loin, the kidney may usually be removed by the extraperitoneal lumbar route. Occasionally, however, it is the operation of choice. When large tumors are to be extirpated, it is wise to expose the renal pedicle by the trans-

peritoneal route and then remove the kidney through the loin. Removal of the diseased organ entirely by the transperitoneal route is not difficult, but should be reserved for cases in which there is no chance of infecting the peritoneum.

All operations upon ectopic kidneys must necessarily be performed through the peritoneum (Operative Treatment of Ectopic Kidney, p. 1694). We have removed a very large pyohydronephrotic ectopic kidney by the transperitoneal route without mishap. The actual removal of such an organ is beset with some technical difficulties, which are not insurmountable when one takes note of the fact that all ectopic kidneys have abnormal blood vessels coming from the nearest great vessels, and these must be ligated as they are encountered.

Postoperative Care Following Nephrectomy. Following nephrectomy, the patient should be observed closely for signs and symptoms of shock, hemorrhage, and abdominal distention. For the first 24 hours, fluids taken by mouth are supplemented by normal saline solution and 5 per cent glucose intravenously, or saline solution by hypodermoclysis, or tap water in 250 cc. doses by rectum. Thereafter, hot clear fluids are given, followed by soft and regular diet as tolerated.

The patient should be turned frequently, usually toward the side operated upon, in order to promote better drainage and counteract any tendency to hemorrhage. Turning also helps to prevent abdominal distention. The back should be supported by a large pillow.

The drains are usually removed on the third or fourth postoperative day, and the patient is kept in bed for from 14 to 21 days.

When clamps are left in the incision following nephrectomy, great care must be taken to see that no pressure is placed on them. Under no circumstances must the clamps be touched by anyone but the doctor. If the clamps are in a right-sided incision, the patient lies on his left side, and vice versa. A pillow is placed against the patient's back, in such a way as not to put pressure on the wound; and a cradle is placed over the patient to keep the bedclothes away from the clamps.

Nephro-Ureterectomy

Under ordinary circumstances, at the time of nephrectomy the ureter is ligated, the cut end treated with carbolic acid and alcohol, and the lower portion dropped back into the loin. In cases of papillary carcinoma of the kidney pelvis, and in certain cases of tuberculosis, in which the ureter is greatly involved, it is advisable to do a complete ureterec-

tomy. In the former, a cuff of bladder tissue around the ureteral orifice should also be removed (Ureterectomy, Figs. 293 to 296).

Nephro-ureterectomy may be accomplished by extending the ordinary lumbar incision downward in the nipple line, or, if deemed advisable, by making a second incision, such as the Gibson "golf-stick" incision in the lower quadrant on the involved side, or the lower midline incision. The kidney and upper portion of the ureter are mobilized through the regular lumbar incision, the kidney with the ureter attached being left hanging from the wound. The patient is then placed in such a position that the anterior incision may be made. Through this incision the lower portion of the ureter is freed, ligated, and cut at its point of entrance into the bladder wall. The kidney can then be drawn back and the ureter removed through the posterior incision.

Heminephrectomy

Heminephrectomy is an old operation which has gained renewed interest within recent years. It was originally performed on diseased halves of horseshoe kidneys. Czerny, in 1887, resected the lower pole of an anatomically normal kidney, and during the next decade and a half this operation was quite frequently done for various conditions, including stone, hydronephrosis, cyst, tuberculosis, and tumor. The results, however, were generally bad, owing to faulty knowledge of renal anatomy and pathology, and the operation fell into disfavor.

It is now realized that in properly selected cases heminephrectomy is a very useful operation, and is neither unusually difficult nor particularly hazardous.

Indications. Heminephrectomy is indicated in cases of *horseshoe kidney* or *unilateral fused kidney* when tumor, cyst, tuberculosis, or pyelonephritis, pyonephrosis, or hydronephrosis, with or without calculous disease, is limited to one-half of the anomalous organ (Operative Treatment of Fused Kidney, p. 1689).

In cases of *double kidney*, where one segment is destroyed by calculous disease, hydronephrosis, or non-tuberculous infection, and the other segment is free of disease, heminephrectomy should be done, thus saving the functioning half of the anomalous kidney (Operative Treatment of Double Kidney, p. 1693). It is our belief that when tuberculous infection is present in either segment of a double kidney, nephrectomy is advisable, if the kidney on the opposite side is functionally adequate. There are

other authors, however, who feel that when a tuberculous infection is limited to one segment of a double kidney with complete duplication of the ureter, resection of the diseased portion only should be done

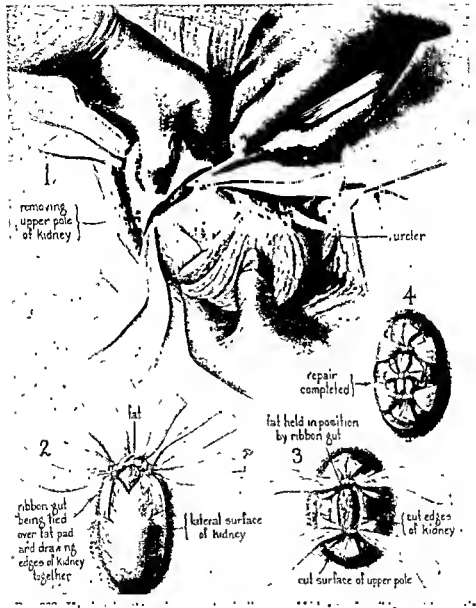
In *anatomically normal kidneys*, heminephrectomy, or partial resection of the kidney, is indicated when one pole is destroyed by stone or non-tuberculous infection but the remainder of the kidney can be demonstrated to be healthy and capable of sufficient function to warrant its conservation. Localized renal destruction due to calculus is the chief condition for which heminephrectomy is now being done. Anything but complete nephrectomy is, we believe, inadvisable in cases of renal tumor or tuberculosis, except, of course, where there is a solitary kidney or where the function of the contralateral kidney is markedly reduced. In such cases, if operation is to be performed at all, it must be a heminephrectomy.

Technic of Heminephrectomy in an Anatomically Normal Kidney. The technic of heminephrectomy upon a horseshoe kidney has been described on page 1691, and in a double kidney on page 1694

The following is our method of performing heminephrectomy in an anatomically normal kidney:

The kidney is exposed and delivered in the usual manner. The line of incision is then decided upon. Ribbon gut, properly moistened, is placed through the fibrous capsule of the kidney, behind the line of incision, on the anterior and posterior surfaces, and the ends tied (Fig. 339). The diseased portion of the kidney is resected in such a manner as to leave a shallow V-shaped wound, the apex of the V being toward the center of the organ. Bleeding is controlled by an assistant grasping the renal pedicle between the thumb and forefinger. A piece of fat is applied to the cut surface of the kidney, and the ends of the ribbon gut are tied together over it with sufficient pressure to control bleeding but not so tightly as to cause pressure necrosis or tear the fibrous capsule through which the ribbon gut has been threaded.

The kidney is replaced in the renal fossa and one or more Penrose drains are inserted in the wound. The wound is closed in the usual manner, using a continuous No. 2 chromic catgut suture for the transversalis fascia and transversus abdominis muscle, interrupted No. 2 chromic catgut sutures for the internal and external oblique muscles, a continuous No. 2 chromic catgut suture for the deep fascia, and interrupted black silk Stewart sutures for the superficial fascia and skin.



Nephrotomy

Nephrotomy is incision into the kidney substance, usually for the removal of calculi, but also for exploration, the repair of injuries, the re-

removal of necrosed areas, etc., or for the establishment of temporary or permanent direct drainage of the kidney (*nephrostomy*).

Use of Ribbon Gut. Considerable renal impairment follows nephrotomy by the customary method, which necessitates the placing of mattress sutures through the renal cortex to obtain approximation of the edges of the incision and at the same time to control hemorrhage. Sutures thus placed must necessarily compress the vessels supplying the cortical and medullary substance of the kidney. Because the vessels are terminal, this cuts off the blood supply of an area extending from the site of the suture to the cortex of the organ, thereby producing an ischemia, with resultant necrosis and scarification of a goodly portion of the kidney. This may amount to as much as 25 per cent of the entire functioning tissue, if the wound is a large one.

This destruction of the kidney substance has been largely obviated in our practice by the use of ribbon gut for the repair of the kidney following operative or traumatic wounds, as reported by Lowsley in 1933 and 1935. This absorbable suture material, which is broad and flat like a ribbon, can be so placed about the kidney as adequately to approximate the incision and control bleeding. The gut is maintained in the desired position for closure of the wound by being passed through the fibrous capsule of the kidney. If properly tied around the kidney, it causes no pressure necrosis.

Hemostasis is accomplished by inserting a strip of fat in the wound and approximating the wound edges without undue pressure. It is amazing how promptly the pad of fat, under a little pressure, will control even profuse hemorrhage in the kidney. This method of controlling bleeding was proposed by Irving Koll, of Chicago, in 1921, and has been very successful in our hands. We have utilized bits of muscle and pieces of fat in the same kidneys under identical conditions, and noted that the former took 16 to 21 minutes to control bleeding, while the fat averaged $\frac{3}{4}$ to $1\frac{1}{2}$ minutes. Microscopic studies by others have demonstrated the thoroughness with which small particles of fat are incorporated in healed wounds of the kidney. Fat has an additional value in that, being semi-fluid, it promptly plugs up the fistulous tract when the drainage tube is removed from the kidney pelvis. Leakage from the nephrotomy wound is, therefore, minimal.

A series of experiments with this technic was first conducted upon rabbits, and served to demonstrate the practicality of the method. The rabbit's kidney is so small that it was deemed advisable to use larger

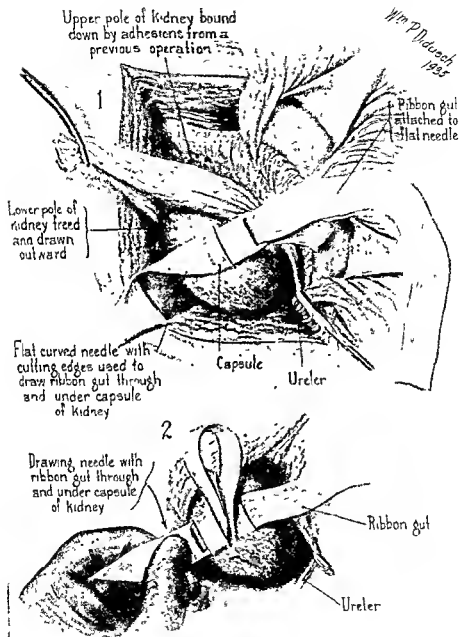
animals. Consequently, dogs were used in the second series of experiments. Their kidneys, while much smaller than the human, are large enough to accomplish the surgical measures involved. Postmortem specimens of animal kidney showed conclusively that wounds and incisions repaired in this manner heal perfectly, and that there is no destruction of kidney, such as one sees when needles are passed through the cortical substance in the usual manner.

The suture material used in this technic consists of flat ribbons of untwisted gut, 25 to 65 cm. long, 1.8 to 2.0 cm. wide, and of the thickness of fine rice paper. The gut is sterilized by heat in the usual type of aseptic catgut tube, and is unaffected by age, climate, or light. Before it is used, ribbon gut should be immersed in warm sterile water or saline solution for about 10 minutes to render it soft and pliable. Unlike the spirally twisted strands of surgical catgut which lose tensile strength by too long an immersion, ribbon gut is not injured by prolonged wetting. It is tied in the same manner as are ordinary types of catgut. The width of the material does not interfere with adequate knots, and the tape shows a tendency to twist only over a distance of about a centimeter immediately adjacent to the knot.

Ribbon gut has several distinct advantages. It is an animal membrane, very soft and pliable, which permits the ingrowth of fibroblasts from surrounding structures between its own fibrils. It may be made ready for use in the operating-room in unlimited amounts at a moment's notice. It is fitted with an atraumatic needle. It possesses the high safety factor of heat sterilization.

Technic. The kidney is exposed and mobilized in the usual manner. When the operation is being done for the removal of a stone, or stones, a polar incision is usually made. Almost any stone may be removed through a polar incision, and this type of wound is more easily repaired than a central cortical incision. The incision is usually made on the lateral, convex border of the kidney, slightly toward the posterior portion of the convexity, so as to avoid the vessels as much as possible.

With the kidney completely exposed, ribbon gut which has been threaded into the Lowsley ribbon gut needle (a short, flat, slightly curved, spear-pointed needle with cutting edges), is fixed in the proper position by passing it through the fibrous capsule of the kidney on the anterior and posterior surfaces (Fig. 340). Having placed the ribbon gut, an incision is made through the renal cortex, hemostasis being secured by manual pressure over the renal pedicle applied by an assistant. Some



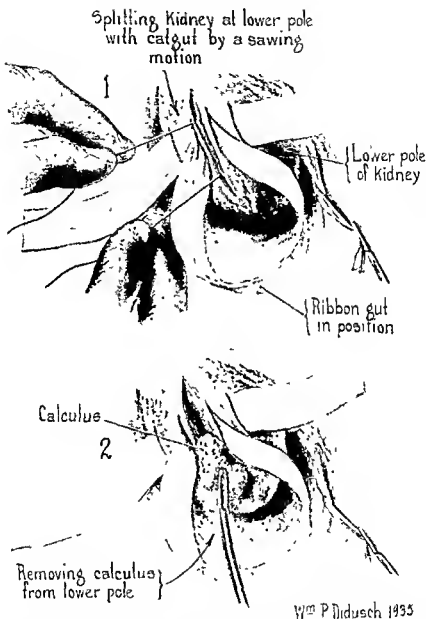


FIG. 341 Nephrotomy. (1) The ribbon gut has been placed in position. Incision is made into the cortex between the two capsular straps (or the kidney may be split with catgut by a sawing motion, as shown here). (2) The calculus is being removed from the upper pole through the incision in the lower pole.

surgeons prefer to incise the kidney by means of a piece of catgut, which is threaded through a liver needle. The catgut is sawed back and forth in such a manner as to incise the cortex. Because of the terminal char-

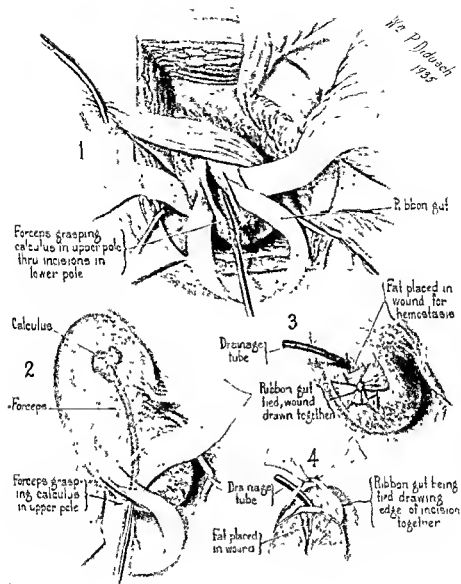


FIG. 342. Nephrotomy. (1) The calculus has been removed from the lower pole. The forcens grasps the calculus in the upper pole through the lower pole incision.

acter of the circulation of the renal cortex, it is assumed that bleeding will be less than if the incision were made in the opposite direction.

The calculus or calculi are located and extracted with forcens.

A drainage tube is inserted through the wound into the renal pelvis.

A piece of fat, suitable to the size of the nephrotomy wound, is placed in the wound for hemostasis and held in position while the ends of the ribbon gut are tied with just sufficient pressure to approximate the edges of the wound. Greater pressure is unnecessary and is to be avoided, since it is likely to result in necrosis. Catgut is fixed in the edge of the ribbon gut and tied around the drainage tube to prevent its dislodgment.

The kidney is replaced in the renal fossa. Penrose drains are placed down to the site of the nephrotomy, and the wound closed in the usual

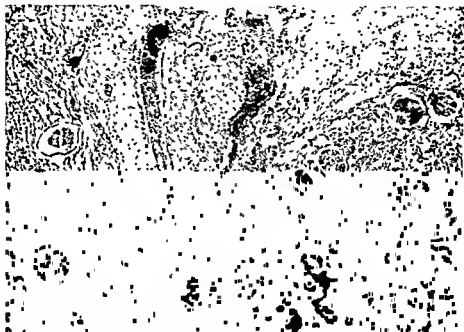


FIG. 343. Nephrotomy: repair of kidney with ribbon gut. Photomicrograph (high power) of a section of the kidney (dog), showing clearly that the glomeruli are normal right up to the edge of the scar. This indicates that there is practically no compression necrosis if the ribbon gut is properly tied around the kidney.

manner, the nephrostomy tube being anchored in place at the posterior angle with one interrupted dermal suture of silk.

As stated before, almost any stone may be removed by means of a polar incision. The entire kidney may be carefully searched, and all fragments removed by forceps or by forceful irrigation with hot saline and suction. We have performed this operation many times for the removal of stones from the renal pelvis or calyces, some of which have been very large.

Operative Roentgenography. Operative roentgenography may be advantageously used in this operation, as the x-rays are of material assist-

ance in detecting stones or fragments of stone which might otherwise be overlooked, thereby reducing the incidence of recurrences. In the interval between preliminary examination and operation, small calculi, which have been observed in the preoperative film, not infrequently move to unexpected places. Prior to the advent of operative roentgenography and fluoroscopy, such stones were either left behind or discovered only after extensive exploration of the kidney, with corresponding injury to its substance.

Postoperative Care Following Nephrotomy. The patient should be turned toward the side not operated upon and supported in back with a large pillow. The special nursing points to be observed in these cases are: (1) to watch and chart the drainage carefully; (2) to see that there is no traction on the drainage tube, and that the rubber tubing does not become kinked and drains freely; (3) to watch for the appearance of blood, mucus, pus, or any other foreign elements in the urine.

Irrigations are given in order to keep the tube open and draining freely. The solutions most frequently used are sterile, distilled water, normal saline, and boric acid, 2 per cent. In stone cases, a citrate solution (see p. 1617) is often used.

The Penrose drains are usually removed 2 to 4 days postoperatively, and the nephrostomy tube in about 10 days. The patient is usually kept in bed for from 12 to 16 days.

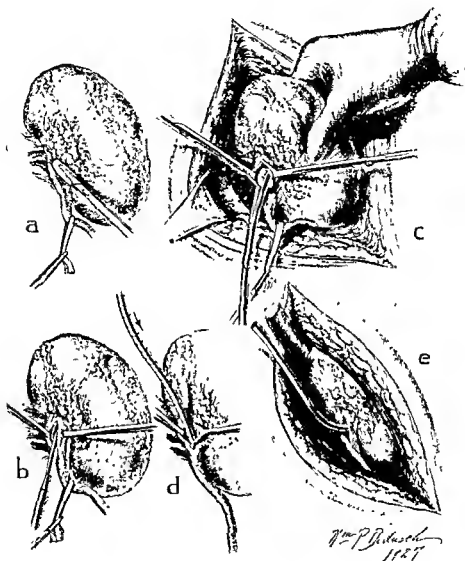
Pyelotomy

When incision of the kidney is confined to the renal pelvis, the operation is termed *pyelotomy*. This is most frequently done for the removal of calculi or for the drainage of hydronephrosis (*pyelostomy*).

Because the majority of renal calculi are located in the renal pelvis or the calyces, pyelotomy is regarded by many operators as the procedure of choice for the removal of most renal stones. In our clinic, pyelotomy was formerly the operation most frequently performed, but, due to the efficiency of the ribbon-gut method of repairing nephrotomy wounds, nephrotomy has now become the operation of choice in most of our cases, and pyelotomy is seldom performed unless the renal pelvis is very large. General bad results from pyelotomy, due to stricture after the operation, with subsequent loss of the kidney, have strengthened our belief that this is an operation which should rarely be performed.

Technic. Figure 344 shows a simple method of performing pyelotomy for the removal of small stones.

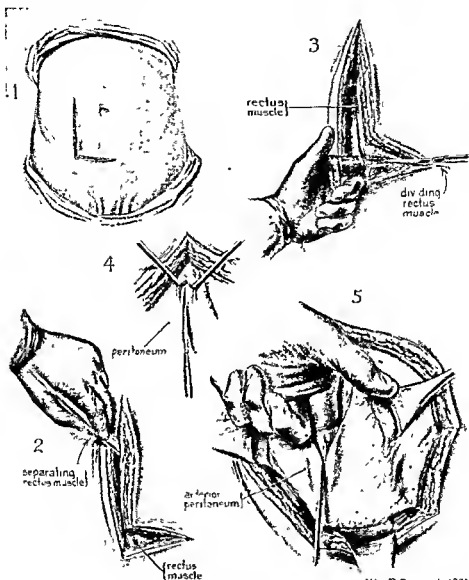
The kidney is exposed, mobilized, and delivered in the usual manner. A tape, passed under the isolated ureter, facilitates its manipulation.



unsutured, although it is safer to set in a suture or two against urinary leakage.

A small incision is made in the pelvic wall at the junction of the ureter, over the stone if possible. Should the incision reach all the way to the

hilum, there is danger of profuse hemorrhage. This short incision gives little room for exploration. A probe can be passed through it into the

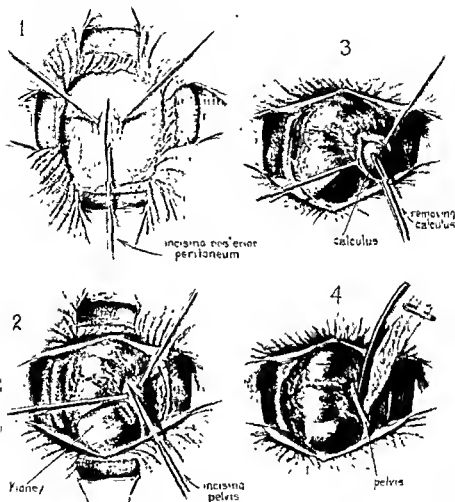


Wm P Didusch 1930

FIG. 345. Transperitoneal pyelolithotomy in ectopic kidney. (1) An incision is made along the outer border of the rectus muscle and then across the rectus. (2) Separating the rectus muscle. (3) Cutting across the rectus. (4) Enlarging the incision in the anterior peritoneum.

ureter, but there is no access to the kidney itself, and even the calyces can hardly be reached. Such an incision is easily closed, however, and, if there is no infection, may be left unsutured, although it is safer to

set in a suture or two against urinary leakage. When leakage is especially to be feared, a flap of fatty capsule is brought down and sutured over the original stitches. The pelvis is drained with a soft rubber tube, which is held in position by a chromic catgut suture.



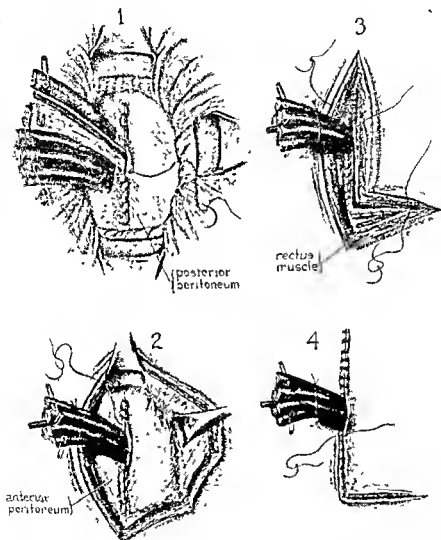
Wm P. Dumas 1130

FIG. 346. Transperitoneal pyelolithotomy in ectopic kidney. (1) Incising the posterior peritoneum. (2) Making an incision in the renal pelvis, which in these cases is anterior. (3) Removing the calculus. (4) A drainage tube is placed in the pelvis, and held there by a chromic catgut suture.

The kidney is returned to the renal fossa, a Penrose drain inserted down to the site of the pyelotomy, and the wound closed in the usual manner.

Postoperative Care Following Pyelotomy. This is the same as for nephrotomy (p. 1679).

Transperitoneal Pyelolithotomy in Ectopic Kidney. Pyelotomy in an ectopic kidney presents an interesting surgical problem. We have performed this operation upon 3 patients within the past 5 years for the removal of renal stones.



Wm P Didusch 1930

FIG. 347. Transperitoneal pyelolithotomy in ectopic kidney. (1) The posterior peritoneum. (2) Penrose drains. (3) Suturing the rectus.

The only approach is by the transperitoneal route (Operative Treatment of Ectopic Kidney, p. 1694). An incision is made along the outer border of the rectus muscle, then continued across the rectus (Fig. 345).

The intestinal tract is carefully packed off and the posterior layer of the peritoneum incised. The stone is usually easily located, as the pelvis in these cases is anterior. Pyelotomy is performed, the stone being removed with forceps. A tube is inserted into the pelvis for drainage and held there by a chromic catgut suture. The posterior layer of the peritoneum is closed around the drainage tube, which is surrounded by Penrose drains. The parietal peritoneum is closed around the tube and drains. The wound is then sutured in layers, and the tube connected with a drainage bottle. The drains may gradually be withdrawn as soon as a fistulous tract is established. A catheter is inserted into the renal pelvis through the ureter before the drainage tube is withdrawn.

Bisection of the Kidney

Bisection of the kidney, for the removal of very large stones, may now be done without hesitancy, due to the efficiency in producing hemostasis which is afforded by the ribbon-gut method of renal repair. By use of the flat needle, ribbon gut may be placed in any part of the kidney and held in the proper position by being threaded through the fibrous capsule. Care must be taken not to have pressure exerted on the renal pelvis or pedicle by the strands of ribbon gut, as considerable damage may thereby be caused to the kidney. A drain is invariably introduced into the renal pelvis, and fat applied on the bleeding surface of the cortex, as described under Nephrotomy (p. 1674). The slight amount of pressure necessary to produce hemostasis does no damage to the cortex, and there is no danger of secondary hemorrhage, as the renal fat is incorporated in the repair of the kidney and necrosis does not occur.

Calyceal Resection

During the past 8 years, at the Brady Foundation, selected cases of primary and recurrent calyceal calculi have been treated by resection of the stone-containing calyx (usually the inferior calyx) together with a wedge-shaped piece of kidney parenchyma—repair of the wound being by the fat and ribbon gut technic. Our experiences with this procedure were reported by Twinem in 1940, and by Yunck and Forsythe in 1941.

Most calyceal stones are removed through either pyelotomy or nephrotomy incisions. In these procedures, however, the infundibulum is often injured, and subsequent stricturing leads to stasis, infection, and stone recurrence. These aftermaths may frequently be prevented by calyceal resection. Healing following this operation is prompt, with little danger

of a permanent urinary fistula; resistant infection is usually not a factor; and there is little decrease, postoperatively, in the function of the kidney, as shown by a comparison of the preoperative and postoperative urea and phenolsulphonphthalein determinations. Most of the patients show no recurrence of stone either at the operative site or in other calyces.

From the animal experiments of Yunck and Forsythe, it would appear that resection of the calyx with the scalpel is definitely superior to resection with the high-frequency cutting current.

Technic. The kidney is exposed through the usual lumbar incision and carefully delivered, the ureter, pelvis, and renal pedicle being gently freed from the surrounding areolar tissue. A wedge-shaped section of cortical and medullary tissue, containing the involved calyx and the stone, is removed in a radial manner in order that the interlobular blood vessels in the remaining parenchyma will be injured as little as possible. The surgical defect is approximated over a small piece of fat by ribbon-gut sutures placed through the fibrous capsule in the manner described for nephrotomy. A large nephrostomy tube is placed in the renal pelvis, and a No. 8 or 9-F. splinting ureteral catheter is bluntly inserted through a separate nephrostomy opening, approximation by suture usually being unnecessary. The wound is closed in layers with drainage.

Postoperative Care. The ureteral catheter is removed at the end of a week, and the nephrostomy tube 3 to 5 days later. The latter is irrigated only when necessary to secure good drainage.

Nephrostomy and Pyelostomy for Temporary or Permanent Drainage

Drainage of the kidney, by nephrostomy or pyelostomy, frequently is indicated as a temporary and preparatory measure. Occasionally, permanent direct drainage is required—as, for example, when both ureters, or a remaining ureter, are diseased or strictured beyond the possibility of repair. A fistulous opening directly through the kidney substance into the renal pelvis has been found much more satisfactory than indirect drainage around the kidney into the pelvis, since nephrostomy tubes must be left in place and changed periodically.

Indications for nephrostomy are:

- (1) Failing renal function due to stricture, occlusion or obstruction of both ureters or a solitary ureter, as in calculous anuria, tuberculosis, and malignant disease.
- (2) Anuria from acute nephritis of mercurial poisoning.
- (3) Dynamic disturbances of the renal pelvis, ureters, and bladder, preventing evacuation of the urine.

- (4) Bilateral renal calculi, with severely damaged kidneys.
- (5) As a temporary measure to improve function, in hydronephrosis or infected hydronephrosis, in which the cause of the obstruction is removable.

Incision and Drainage of Renal Abscess

A large, well-walled-off renal abscess of non-tuberculous origin, which does not involve too much of the renal substance, may often be successfully incised and drained, thereby saving a functioning organ.

Technic. The kidney is exposed in the usual manner but is not isolated, as it is advisable not to expose any more tissue than is necessary to drain the abscess. The lesion, having been located, is punctured with scissors or a hemostat. A drainage tube is inserted in the abscess cavity and fixed in position with a plain catgut suture. Penrose drains are inserted down to the kidney and the wound closed in layers, but not too tightly.

Postoperative Care. The drainage tube is irrigated daily with a suitable antiseptic solution such as: peroxide-iodine solution (3 or 4 drops of iodine to each 60 cc. of peroxide), Dakin's solution, full or half strength; potassium permanganate, 1:10,000; normal saline solution, and boric acid, 2 per cent. When the drainage ceases, the Penrose drains are first removed, the tube later, and the wound finally allowed to heal.

Operative Treatment of Renal Cysts

Polycystic Disease. The treatment of polycystic disease is largely medical (Polycystic Disease, p 1537). The condition is always bilateral and progressive, and no operation as yet devised will influence more than temporarily the growth of the cysts and the destruction of the renal tissue. Operative removal of the more advanced kidney will not improve its polycystic mate; on the contrary, nephrectomy appears to hasten cystic degeneration in the opposite kidney, and in a majority of cases has ended disastrously. Although urological opinion is practically unanimous that a polycystic kidney should not be removed because of its cystic condition alone, opinions differ regarding removal of a polycystic kidney that is otherwise diseased. Some authors feel that nephrectomy is never justifiable, while others are of the opinion that if the polycystic condition of one kidney is complicated by a surgical lesion, such as tumor, stone, or gross infection, which presents a direct threat to the patient's

life, and the function of the opposite polycystic kidney is adequate to sustain life, nephrectomy should be done, even though the remaining kidney will progressively enlarge and eventually fail.

It is our opinion that removal of a polycystic kidney is rarely indicated but that occasionally conditions do occur which warrant the performing of nephrectomy. Dr. Roy B. Henline has reported a very interesting case of fibrosarcoma in a polycystic kidney successfully treated by operation, the patient doing well for 5 years after operation, with the opposite kidney functioning adequately to permit her to lead a normal life. This 46-year-old woman was first admitted to the Brady Urological Foundation, of the New York Hospital, in 1933, complaining of intermittent blood in the urine. Following a complete urological study, removal of the right kidney was advised. Operation was refused by the patient at this time and on several subsequent admissions. The kidney, with the tumor, was finally removed in 1936 by Dr. Henline. The vena cava was almost occluded by the tumor, but by careful dissection and manipulation the tumor mass was delivered from the vena cava with very little bleeding. For 5 years the patient did well, but at the present time (6 years post-operatively) there are widespread metastases.

Conservative operative measures are sometimes necessary for the relief of hemorrhage or infection. Bleeding from a polycystic kidney, either through the pelvis or in the perirenal region, may be so great that operation must be done as a life-saving measure. Occasionally a polycystic kidney may become so grossly infected that a nephrostomy is necessary. We no longer fear to do a nephrostomy in such cases, since the bleeding is easily stopped by applying pieces of fat over the bleeding points and holding them in place with ribbon gut. One patient in our experience lived 10 years after a nephrostomy necessary to control the bleeding from one of his kidneys, and died at the age of 67 years. Nephropexy or plastic operations for the securing of better drainage may occasionally be advisable. In a case of bilateral polycystic disease observed at the Brady Foundation, Twinem incised and drained a perinephritic abscess on each side, the patient eventually being able to resume his occupation as a fireman.

In selected cases, puncture of the cysts, as recommended by Rovsing many years ago, has a beneficial effect on general symptoms and, to a certain extent, controls pain, hemorrhage, and infection. As many cysts are evacuated as can be reached by surgical exposure of one or both kid-

neys. We favor the insertion of a nephrostomy tube, which is only removed when the urine is cleared of both pus and blood. Penrose drains are inserted to the site of the punctured cysts to carry off the secretions.

If operation of any type is to be undertaken upon a polycystic kidney, the presence of an adequate functional reserve in the other kidney must be very carefully established. The avoidance of general inhalation anesthetics in surgery upon the polycystic kidney is most important.

Simple Cysts. The treatment of choice in the majority of cases is excision of the free portion of the cyst, with treatment of the adherent remainder by phenolization, and closure of the defect with a pad of fat and chromic ribbon gut, as described below. Attempts to remove these cysts *in toto* are likely to result in a dangerous amount of bleeding, due to the firm adhesion of a portion of the cyst wall to the renal parenchyma. Resection of the free portion of the cyst by the method described here is a practically bloodless operation, and there is little likelihood that the cyst will recur following this procedure.

Nephrectomy is reserved for cases in which there is marked destruction of the kidney either by the cyst or by associated disease, or in which careful examination of the cyst wall at operation discloses evidence of malignancy. Neoplasm should always be suspected, and thoroughly searched for, when the contents of the cyst are hemorrhagic.

If the patient refuses operation, or if surgery is for any reason contraindicated, aspiration of the fluid content of the cyst through the loin, and the injection of 50 per cent glucose solution, will give relief from pain and may, in an occasional case, even result in cure.

Excision of Free Portion of Cyst, with Phenolization, and Repair of Kidney with Fat and Ribbon Gut. The kidney is exposed through the usual lumbar incision, and the cyst carefully freed by blunt dissection. The free portion of the cyst is then excised. The smooth lining of the remnant of the cyst wall in contact with the renal parenchyma is not removed. Fifty per cent phenol with glycerine is applied to the lining of this unexcised portion of the cyst wall, and is followed by the application of 95 per cent alcohol.

The defect in the kidney caused by the removal of the cyst is repaired as follows: A pad of fat is placed in the residual cavity for hemostasis, and the margins of the kidney are closed over the fat with mattress sutures of chromic ribbon gut placed through the fibrous capsule of the kidney.

Operative Treatment of Hydronephrosis

The operative treatment of hydronephrosis has been adequately covered elsewhere in these pages (Hydronephrosis: Treatment, p. 1420; Surgical Treatment of Obstructions at the Ureteropelvic Junction, p. 1305).

Incision and Drainage of Perinephritic Abscess

Technic. A small incision is utilized in draining a perinephritic abscess. It extends for about 7 cm. along the lower border of the twelfth rib. It is deepened through the subcutaneous tissue and musculature, and the deep fascia is then incised. The fatty capsule—the site of the abscess—lies just beneath the deep fascia.

An instrument is inserted, and the abscess thus opened is drained by suction. A specimen of pus is secured for culture. The interior of the abscess is then explored with the finger, and any honey-combed areas and pockets are broken down. Care is taken not to break through the wall of the abscess, thus preventing extension of the pyogenic process.

After the abscess cavity has been thoroughly cleaned out, a tube, split at its lower end, is inserted.

The wound is closed in the usual manner, but not too tightly as this might interfere with proper drainage.

Postoperative Care. The wound is irrigated at frequent intervals with suitable antiseptic solutions (see Renal Abscess, p. 1686). After drainage ceases, the application of heliotherapy and ultraviolet light will stimulate healing.

Operative Treatment of Renal Anomalies

The surgical treatment of renal anomalies has already been considered to some extent (Anomalies of the Kidney, p. 1361; Surgical Treatment of Ureteral Anomalies, p. 1302).

The three types of anomalous kidneys which most frequently require operative treatment are: (1) fused (horseshoe) kidney, (2) double kidney, and (3) ectopic kidney.

OPERATIVE TREATMENT OF FUSED KIDNEY

Fused kidneys, because of their anomalous position and blood supply, are much more likely to be the site of pathological change than non-fused

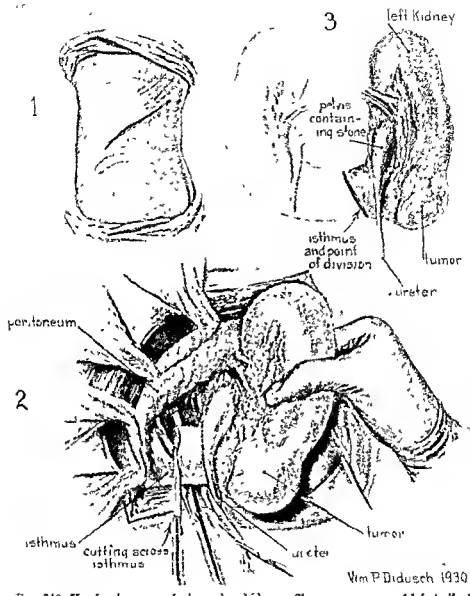
organs (Fused Kidney, p. 1373). The most common types of pathology are hydronephrosis, calculus, and infection. Tuberculosis, cysts, and tumors are not infrequent. In a case reported from our clinic, the left half of the horseshoe kidney was the seat of a calculus, a papilloma, and a hypernephroma the size of a small tangerine (DeVries, 1930). A heminephrectomy was successfully done in this case. Once a horseshoe kidney, or other form of fused kidney, has become diseased, there is usually slight chance of permanent cure except by surgical intervention. Palliative measures may afford temporary relief in some conditions, but recurrence is the rule because of poor drainage due to the high insertion and abnormal course of the ureters and the presence of aberrant vessels.

Calculus may require pyelotomy, ureterotomy, or nephrotomy for its removal. Division of the isthmus, with nephropexy when necessary, has been advocated for certain cases of pathological change due to back pressure.

Heminephrectomy is often indicated when the pathological process is limited to one-half of the fused kidney, and has been successful in our hands in several instances. The first surgeon to attempt removal of the diseased half of a horseshoe kidney appears to have been Braun (1882). The operation was not successful. In 1888 Socin succeeded in curing a patient suffering from intermittent hydronephrosis by first opening the dilated kidney pelvis, and later, when relief was not afforded, by resecting the affected half of the kidney. During the opening decade of the twentieth century, heminephrectomy was successfully performed by numerous operators for various types of pathology in fused kidneys, and from then on heminephrectomy in the diseased horseshoe kidney became fairly common. In 1928 we were able to collect 92 cases from the literature.

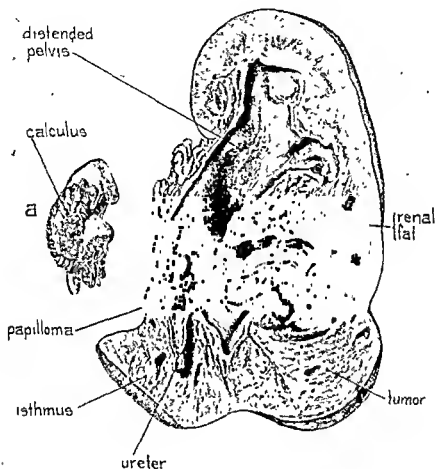
Operations upon fused kidneys present more problems than similar procedures upon non-fused organs, but, prepared by accurate diagnosis and knowledge of the state of both portions of the fused kidney, the surgeon can usually attack pathological conditions in these organs with the same hope of success as when the lesions are situated in normally formed and located organs.

If both sides of the fused kidney are diseased, surgery is limited to palliative treatment, and even this must be undertaken with extreme caution.



Heminephrectomy in Horseshoe Kidney. The kidney is exposed by an incision parallel to and below the twelfth rib, extending from about

the middle of the rib to a point above the anterior-superior spine of the ilium. Care is taken to avoid injury to the twelfth nerve and its branches, and to the ilio-inguinal and ilio-hypogastric nerves. Occa-



Wm P Didusch 1924

sionally a branch of the twelfth nerve will extend across the incision. When this happens, careful dissection will often allow the nerve to be retracted to the proximal side of the wound.

The fascia covering the erector spinae muscles is incised both above and below the point where it participates in the formation of the costovertebral ligament. This allows the rib to swing up, and makes rib resection unnecessary in most instances. The fascia is incised, the muscles divided, and the deep fascia nicked in the costovertebral angle. This incision is widened and the peritoneum carefully protected as it is stripped back. If the peritoneum is accidentally injured, it is immediately repaired.

The fatty capsule surrounding the kidney is then grasped well up in the costovertebral angle and opened. This opening is enlarged by blunt dissection until the cortex of the kidney is seen. The fatty capsule is then separated from the kidney. During this process it will be found necessary to tie off many aberrant blood vessels, which are always present in horseshoe kidney and may come from any nearby large vessel.

Having separated the upper pole of the diseased half of the horseshoe kidney and secured the bleeding points, the ureter is then dissected down as far as possible, and the stump ligated and incised with a cautery or with scissors, the cut ends being cauterized by carbolic acid followed by alcohol.

The dissection is continued, and any vessels encountered are secured. The isthmus is identified and freed from surrounding adhesions. The diseased portion of the horseshoe kidney is then excised by making a V-shaped incision into the isthmus, the apex of the V pointing toward the sound half. After removal of the excised portion, the isthmus is repaired by means of ribbon gut (which has previously been placed through the fibrous capsule), a small piece of fat being held in the V-shaped wound while the ribbon-gut ends are being tied over it.

Penrose drains are placed down to the isthmus, and the wound is closed by layers, plain catgut being used except in the skin, where silk or silk-worm gut is used in interrupted sutures.

Postoperative Care. The postoperative care is that usually given to nephrectomy cases.

OPERATIVE TREATMENT OF DOUBLE KIDNEY

Double kidney—namely, an organ with two pelves, with or without separate ureters—has already been considered in connection with Anomalies of the Ureter (p. 1215) and Surgical Treatment of Ureteral Anomalies (p. 1302). Such a kidney may have one part badly diseased and of no functional ability. Provided that there is a healthy kidney on the oppo-

site side, it is the practice of many surgeons to do a nephrectomy, sacrificing the good half of the double kidney with the bad.

When a double kidney presents stone, hydronephrosis, or non-tuberculous infection of one segment, with the other segment free of disease, we believe a heminephrectomy should be done, thus conserving an important functioning organ. If either part of the double kidney is the site of a tuberculous infection, nephrectomy is advisable, if the contralateral kidney is healthy, since heminephrectomy in such cases may leave a permanent fistula, and, in any event, removal of the remainder of the double kidney will ultimately be required in almost every case.

Heminephrectomy in Double Kidney. The kidney is exposed in the usual manner and carefully isolated. The distribution of the vascular supply must be carefully determined, since in certain double kidneys the halves have separate blood supplies.

The site of the heminephrectomy is decided upon. Chromic ribbon gut is placed through the fibrous capsule on both the anterior and posterior surfaces, above and below, and the ends tied and left hanging free.

The diseased portion of the kidney is outlined, and is then excised by making a V-shaped incision into the healthy portion, pressure being exerted on the renal artery by an assistant to prevent excessive hemorrhage. A small pad of fat is placed over the cut surfaces, and the ribbon-gut sutures are tied together, approximating the edges of the wound and so compressing the vessels that when the pressure is removed from the vascular pedicle the bleeding is controlled.

OPERATIVE TREATMENT OF ECTOPIC KIDNEY

Surgery in an ectopic kidney is often necessary, and has been done with entire success in many instances. All operations upon ectopic kidneys must be done by the transperitoneal route. Operation is frequently difficult, due to the ever-present anomalous blood vessels. The blood supply of an ectopic kidney comes from the nearest great vessels, and the vessels must be clamped and ligated as they are encountered by the operator. The fact that ectopic kidneys lie directly upon the great vessels makes extreme care essential when severing the adhesions which always surround a diseased kidney. Subcapsular removal is sometimes advisable.

Some authors bluntly state that the only treatment for an ectopic kidney is nephrectomy, which, of course, can only be done when the opposite kidney can unequivocally be demonstrated to be capable of

carrying on alone. Frequently the displaced organ will be so diseased, or at least hydronephrotic, that the normal kidney will be doing most of the work. But if the ectopic organ is so placed that its drainage is fairly good, and if infection is absent, or moderate and capable of control, its conservation should be attempted. If the ectopic kidney is situated above the crest of the ilium, the defects of drainage are sometimes susceptible of correction. This may be accomplished by mobilizing the kidney sufficiently to place it in the normal position, where it may be anchored by sutures. This cannot be done in the case of an ectopic pelvic kidney, because its vessels are derived from the iliac and pelvic plexuses and are so located as to make it impossible to raise the kidney to its natural position.

It is possible to drain the kidney through the peritoneal cavity without danger by using a drainage tube fixed in the renal pelvis and completely surrounded by Penrose drains. These may gradually be withdrawn as soon as a fistulous tract is established. A catheter is inserted into the renal pelvis through the ureter before the transperitoneal drainage tube is withdrawn.

The removal of calculi by pyelotomy is described elsewhere (*Transperitoneal Pyelolithotomy in Ectopic Kidney*, p. 1683).

Operative Treatment of Renal Injuries

Indications for Operative Treatment. While slight, uncomplicated renal injuries will usually heal under palliative treatment, it is our belief that many cases of renal injury are fatal because the surgeon does not operate soon enough. Early exposure in all cases where the extent of the injury cannot be definitely determined is advisable. Early operation enables the surgeon, first, to remove the extravasated clotted blood, which, if allowed to remain, may become infected or result in marked fibrosis, causing obstruction of the ureter and secondary disturbances within the urinary tract. It also enables the surgeon to inspect the kidney and adjacent structures and make the necessary repairs, when possible, thereby saving the kidney. Should nephrectomy be inevitable, it is much better that it be done at once than that the patient be exposed to the dangers of uncontrollable hemorrhage or secondary infection.

We have definitely proved, by experimentation and clinical observation, that great destruction of the kidney may occur without primary rupture of the fibrous capsule. Pulpefaction of a large part of the kidney cortex may occur without any perirenal infiltration of either blood or

Wm. P. D. Jensen (1931)

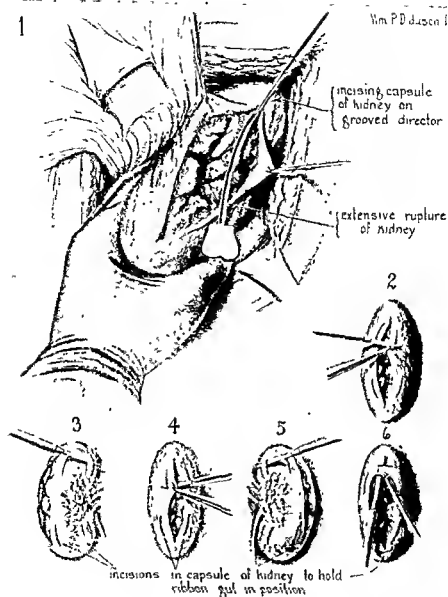
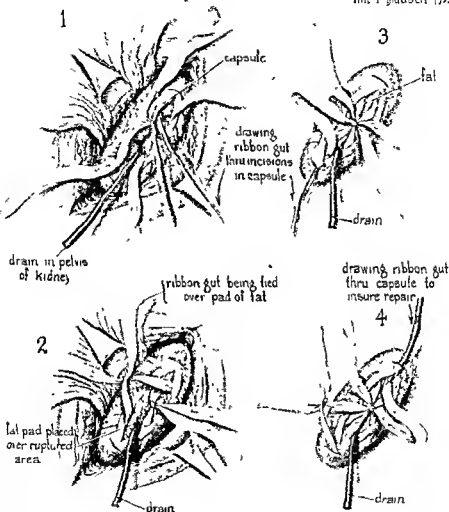


FIG. 259. Repair of ruptured kidney by the use of ribbon gauze. (1) The kidney has been incised. (2) The capsule has been incised. (3) The capsule has been sutured. (4) The capsule has been sutured. (5) The capsule has been sutured. (6) The capsule has been sutured. Blood clots are used in the repair.

urine until many days after the initial traumatism, when the fibrous capsule has been digested by the *ferments* released under it by traumatism to the cortical substance.

We believe that every case of renal traumatism that is sufficiently severe to cause hematuria or pain in the kidney area should be hospitalized and carefully observed. If shock is great, the patient should be

Wm. P. Jidusch 1933



given supportive treatment, including blood transfusion, and exploratory operation done at the earliest safe moment. If there is evidence of extravasation in the intravenous pyelogram, or of extensive hemorrhage,

as indicated by a tumor in the loin, rigidity, hematuria, shock, and by blood examination, immediate exploratory operation should be done and the injury dealt with according to the findings. If the injury has not been grave at the outset, but hematuria continues longer than 24

Wm P Didusch 1933

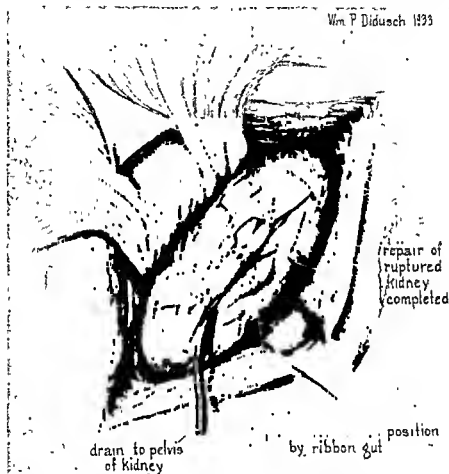


FIG. 352 Repair of ruptured kidney; ribbon-gut method. Repair completed. The pad of fat is held securely in position by the ribbon gut, which is tied over it with sufficient pressure to control hemorrhage.

hours, surgical exposure is indicated. Even if there is no hematuria, but the pulse rate increases, the blood pressure begins to drop, and tenderness and swelling persist in the loin, operative intervention should not be delayed.

At operation, the kidney may be found to be damaged beyond the possibility of successful repair, or there may be involvement of the

vascular pedicle, so that nephrectomy becomes imperative. In emergency cases, where there has been no time to demonstrate a normal kidney on the opposite side, this should be determined by opening the peritoneum through the lumbar incision and direct palpation before the injured kidney is removed. Occasionally, it may be more convenient to approach the injured kidney by the abdominal route, particularly if other injuries have been sustained.

Frequently, even in badly traumatized kidneys, isolated fragments of parenchyma may be removed, the kidney pelvis drained, and hemostasis obtained by introducing small pieces of fat and repairing the capsule by the ribbon-gut method reported by Lowsley in 1933.

Repair of Ruptured Kidney by Ribbon-gut Method. The kidney is exposed in the usual manner and isolated. If the renal damage is extensive, the fibrous capsule will be elevated by the underlying hematoma, and the damage to the renal cortex can be both seen and felt.

The capsule is opened, blood clots are sponged away, and isolated wedges of damaged cortical tissue are removed. Bleeding is controlled by applying small pieces of fat and fixing them in position by tying ribbon gut around the kidney and over the affected portions, sufficient pressure being used to control the hemorrhage. The gut may be fixed in any desired position by means of straps made in the fibrous capsule of the kidney. A rubber drainage tube is passed into the renal pelvis before the ribbon-gut ends are tied.

Penrose drains are placed around the kidney, and the wound is closed in layers in the usual manner.

Operative Treatment of Nephroptosis

Indications for Operation in Nephroptosis. The indications for surgical intervention in nephroptosis have been considered in the preceding chapter (*Nephroptosis: Diagnosis, Treatment, p. 1625*).

Types of Operations. A properly performed nephropexy, with decapsulation, ureterolysis, ureteropyclopasty, or sympathectomy, as required, is productive of highly beneficial results in carefully selected cases. In order to fix the kidney so as to secure free drainage of its pelvis and ureter, abnormalities of the ureteropelvic junction and upper portion of the ureter, which are operating with the renal mobility to impede drainage, must first be corrected. Frequently, therefore, elevation of the kidney is but part of the surgical treatment.

The selection of suitable cases for operation cannot be too often

emphasized. Excessive renal mobility alone seldom produces symptoms, and unless there is evidence of interference with pelvic and ureteral emptying, surgery is rarely indicated.

Exceptions are certain cases of nephralgia, for which we advocate denervation and decapsulation.

The technics for nephropexy, which have been described since Hahn, in 1881, first recommended suspension of the kidney, are almost infinite in number and variety. Most of them fall into one or another of the following groups: (1) partial decapsulation, with the kidney supported by gauze packed below it until adhesions capable of maintaining its position have formed; (2) partial decapsulation, with obliteration by suture of the fascial pocket into which the kidney has become habituated to descending; (3) suspension of the kidney by transfixing sutures of various materials through the parenchyma; (4) the use of flaps from the renal capsule (Morris turns back a wide flap and sutures it to the upper angle of the wound; Vogel uses two strips of capsule from the anterior surface which he wraps around the last rib, brings forward, and sutures to the adherent portion of the capsule); (5) suspension of the kidney as in a hammock. A majority of these operations either subject the kidney to serious infections or destroy a portion of the parenchyma by puncturing sutures.

Brödel's triangular stitch method and Edebohl's operation have been widely copied. Among the many others who have devised methods of nephropexy are Papin, J. J. Bell, O. S. Fowler, Fullerton, von Lichtenberg, Thomson-Walker, Mathé, Deming, and Lowsley. Hess reports a large number of cases of periarterial sympathectomy with ureterolysis, with very satisfactory results, and recommends this procedure even as a substitute for nephropexy.

In our own practice we have had excellent results with the ribbon-gut method of nephropexy described by Lowsley in 1935. We have also found Deming's method of supporting the kidney by a hammock of fascia a satisfactory and practical procedure.

Irrespective of the technic used in performing nephropexy, certain fundamental surgical requirements should be complied with, namely:

- (1) The ureteropelvic junction and upper portion of the ureter must first be freed of all constricting bands, aberrant vessels, etc.
- (2) The kidney should be replaced as nearly as possible in its normal position.
- (3) Changing the axis of the kidney is as important as elevation.

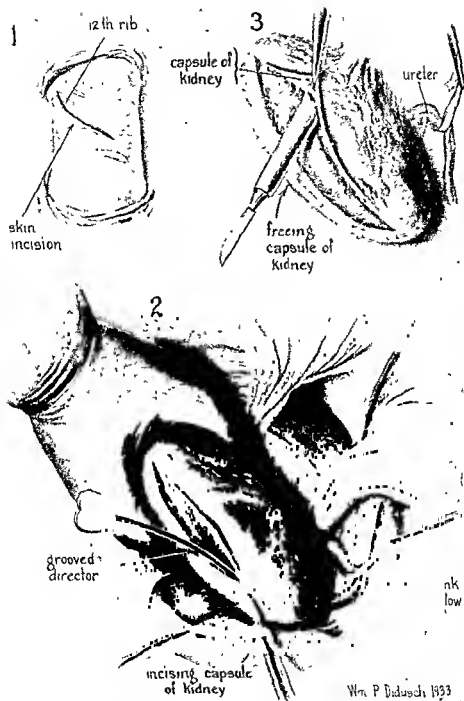


FIG. 353. Nephropexy, using chromicized ribbon gut. (1) Lumbar skin incision. (2) The kidney has been mobilized and delivered. Incising the fibrous capsule of the kidney. (3) Freeing the capsule, so as to expose about one-sixth of the renal surface.

- (4) The kidney must be so placed that the ureter is straight and all kinks and tortuosities removed.

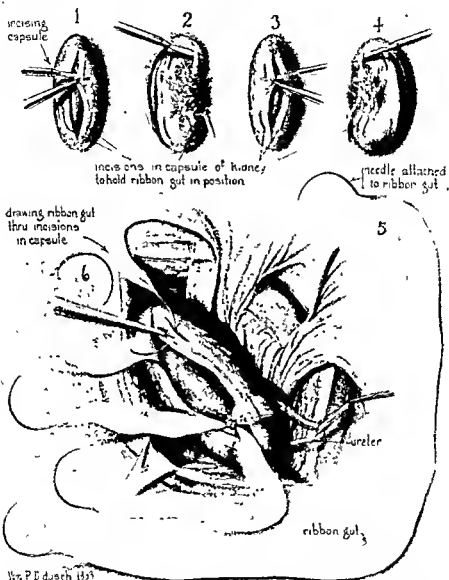


FIG. 354. Nephropexy, with ribbon gut. (1 to 4) Making incisions in the fibrous capsule, at the upper and lower poles, to hold the ribbon gut in position. (5) Chronic ribbon gut with needle attached. (6) The ribbon gut in position about the lower pole. Drawing the gut through the incisions in the upper pole.

- (5) Postoperatively the patient should be kept in the recumbent position, with the foot of the bed elevated, long enough for supporting adhesions to form (usually about 16 days).

Nephropexy by Lowsley's Ribbon-gut Technic. In this technic, 21-day chromacized ribbon gut, studded with an atraumatic needle at each end, is used.

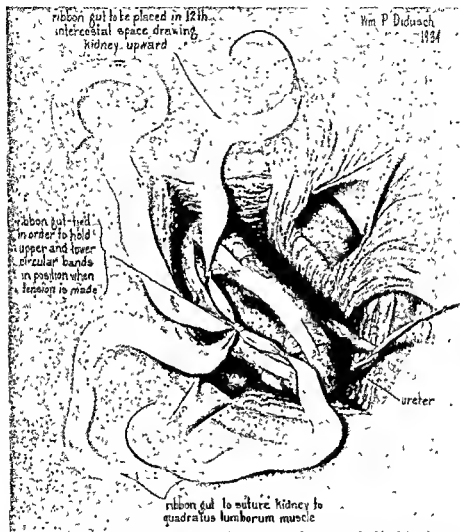


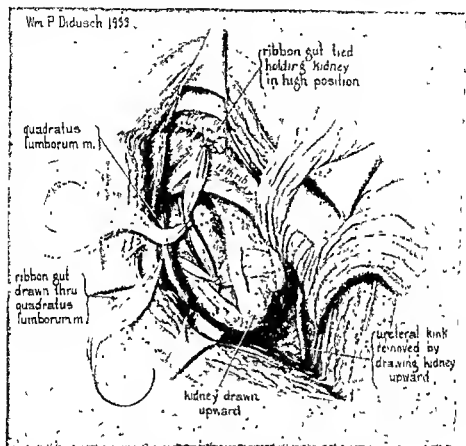
FIG. 355. Nephropexy, with ribbon gut. Showing the ribbon gut in position about the two poles of the kidney. One end of the strand about the upper pole is tied to the free end of the strand about the lower pole to hold the two slings firmly in position when tension is made.

An incision is made about 2 cm. below the costal margin, extending from the costovertebral angle downward and mesially for about 16 cm. This is deepened through the fascia. The costovertebral ligament is incised, allowing the twelfth rib to swing up and giving more operative space. The incision is continued through the muscular wall, care being

taken to preserve the ilio-inguinal and ilio-hypogastric nerves, as well as the lower fibers of the twelfth costal nerve.

The fatty capsule is opened, the kidney mobilized, aberrant vessels or fibrous bands ligated and divided, and the organ delivered.

The fibrous capsule is divided in the midline and stripped back, exposing about one-sixth of the kidney's surface.



tus lumborum muscle.

Chromic ribbon gut is fixed about the upper and lower poles of the kidney, being passed through straps made in the fibrous capsule at suitable intervals. It must be tied loosely enough so as not to cause compression of the cortical substance, but tightly enough to hold firmly. The free ends of the upper and lower strands are then tied together, which helps to hold the ribbon gut in position and forms a basket-like support for the kidney.

The needle attached to the sling of ribbon gut about the upper pole is then inserted just above the border of the twelfth rib, as far back as possible, and the ribbon gut drawn through, bringing the kidney, with its partly denuded cortex, up to the body wall. Care must be taken to pull the kidney sufficiently high so that the ureter, which has been dissected free, is straight and slightly stretched. The attached needle

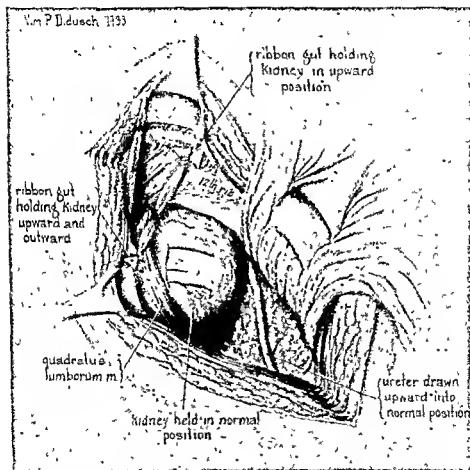


FIG. 357. Nephropexy, with ribbon gut. Operation completed. The kidney is drawn upward and outward, with the ureter free and straight.

is cut away, and this end of the ribbon gut is tied to the end which has been tied to the lower strand of gut. The needle-studded end of the sling of ribbon gut about the lower pole is passed through the quadratus lumborum muscle at an appropriate place, the needle cut away, and the end tied to the end which has been tied to the upper strand.

A careful examination is again made, to be certain that there is no



FIG. 259. Nephropathy with diffuse and focal interstitial nephritis (case of rat kidney).

which has produced inconspicuous damage in the renal parenchyma

obstruction of the ureter, and the wound is closed in layers in the usual manner, without drainage.

Deming's Method of Nephropexy. In Deming's operation the incision is begun high in the costovertebral angle and continued downward and transversely half-way between the lower rib and the crest of the ilium. Approach to the kidney is through Petit's triangle. The twelfth thoracic nerve is located and carefully avoided. The fatty capsule is opened posterolaterally. The perirenal fat is stripped off the kidney, which is then delivered into the wound. Adhesions at both poles must be removed, and the ureter straightened, if kinked or twisted.

The kidney is placed with the upper pole in a median position and the lower pole pointing outward, to provide the lower calyx with dependent drainage. It must be replaced sufficiently high to remove all kinks and tortuosities, which sometimes requires that an adherent right lobe of the liver must first be freed.

With the kidney held in this position, from 5 to 8 interrupted mattress sutures of chromic catgut No. 00 are placed through the perirenal fascia and peritoneum into the quadratus muscle, the first stitch being 1 cm. from the ureter and as high as possible on the quadratus muscle posteriorly. These sutures form a basket sling for the kidney, so that it is impossible for it to descend. This row of sutures is reinforced by bringing up all the retroperitoneal fat and suturing it with 2 or 3 mattress sutures to the quadratus muscle below the first line of sutures. This not only reinforces the original support, but fills up the space formerly occupied by the kidney.

The wound is closed in layers, without drainage, using No. 2 plain catgut for the subcutaneous tissues and interrupted sutures of silk for the skin.

Decapsulation of the Kidneys

Bilateral renal decapsulation—the stripping from the kidneys of the greater part of their fibrous capsules—is quite frequently done in cases of acute diffuse glomerulonephritis, pregnancy toxemia, chronic nephrosis with edema, and bichloride of mercury nephrosis. It is probably not indicated unless there is oliguria or anuria.

Unilateral decapsulation is sometimes performed in nephralgias and acute renal infections.

Semi-decapsulation is usually done in nephroptosis, in conjunction with nephropexy.

Technic of Bilateral Decapsulation. Bilateral decapsulation is rather easily accomplished by the following technic:

The patient is placed flat on the abdomen, with an elevator under the abdomen. This puts the back on the stretch.

The incision extends from the costovertebral angle outward and downward under the twelfth rib, keeping about 2 cm. from the rib in order not to injure the subcostal vessels and nerve. The wound should be sufficiently long to expose the kidney properly.

The kidney is freed from its fatty capsule by blunt dissection. An incision is made through the fibrous capsule on the convex surface, and the capsule stripped back (using the blunt side of the scissors). This exposes the cortex and relieves any subcapsular pressure that may exist.

The wound is closed in layers in the usual manner, without drainage. Identical procedures are done on both kidneys.

Renal Sympathectomy for Nephralgia

Renal sympathectomy is a very useful operation in the rather uncommon cases of true nephralgia with which the surgeon comes in contact.

The idea of severing the nerve fibers conveying impulses provocative of pain or motor imbalance originated many years ago, but it was not until 1921 that renal denervation was practiced upon a human being. This initial renal sympathectomy was done by Papin of Paris, who became convinced that in this procedure he had found a means of relieving the pain due to chronic nephritis and hydronephrosis from various causes, as well as nephralgias of unexplained origin. Herbst, in 1932, and S. H. Harris, in 1935, discussed the scope and utility of renal sympathectomy in America and Great Britain respectively. In 1936 the entire subject was well reviewed by T. E. Gibson, who concluded that the operation has no harmful effects upon the kidney, is surgically feasible either alone or in conjunction with other procedures, and in a number of conditions is indicated for the relief of pain, especially when there is no demonstrable pathology in the kidney to account for the symptoms.

Innervation of the Kidney. The splanchnic nerves are chiefly responsible for carrying painful stimuli in the renal region, and through the celiac ganglion the splanchnics are brought into relation with the vagus nerve. But the vagus nerve does not contain any vasomotor fibers which reach the kidney, nor does it apparently influence the kidney in any way, except indirectly through the heart action. No ganglion cells are found in the renal parenchyma, although they are found in the renal plexus. But in

the splanchnics many vasoconstrictor and vasodilator fibers can be demonstrated—the constrictors greatly outnumbering the dilators. Vasodilator fibers destined for the kidney are to be found in the vagus nerve; and the renal plexus surrounds the renal artery with a somewhat loose investment of nerve fibers, although no corresponding network is found about the renal vein. It has been noted that the kidney may be completely denervated by the performance of a segmental periaarterial sympathectomy.

In addition to the purely vascular innervation, there seems to be a widely extended, non-medulated innervation of the renal parenchyma. In the connective tissue of the walls of most of the renal vessels, and in the smooth muscle found in the renal pelvis and calyces, are to be found motor nerve endings, as well as the terminations of sensory nerves; but there is no collateral innervation. It has been noted that if the splanchnics or the renal plexus of either side be stimulated, vasoconstriction will take place, but only on the same side as that subjected to irritative impulses.

Comparing the work of various surgeons upon renal nerves, T. E. Gibson concluded that the indications for performing renal sympathectomy were the same as those accepted for the use of sympathectomy in any other part of the body, namely: vasomotor spasm, pain; and motor imbalance or dyskinesia. These are all capable of causing renal symptoms which cannot be accounted for by the presence of demonstrable organic lesions. Disturbance of the mechanism of muscular innervation in the kidney was termed by S. H. and R. G. S. Harris "sympatheticotonia." They characterized it thus: (1) positive reproduction of the pain complained of by the patient on distension of the renal pelvis; (2) pyeloscopic demonstration of definitely decreased motility in any of the calyces or of the entire pelvis; (3) delayed emptying time of the individual calyx or pelvis; (4) recurrence of pain after its temporary relief by physostigmine; (5) evidence of generalized sympatheticotonia, which may be most marked on the side of the lesion; (6) negative urinary observations on microscopic and cultural examinations, and (7) the proved absence of organic ureteral stricture.

Indications for Operation. The indications for renal sympathectomy are indefinite, and, until more is known about the relation of the sympathetic nerves to the kidney, will undoubtedly continue so. The operation was originally performed by Papin for chronic painful nephritis, hydronephrosis of small size, and nephralgias for which no cause could be demon-

strated. Hess has recommended the procedure for use in connection with nephropexy, where that operation has failed to relieve the patient of the pain and nervous symptoms accompanying movable kidney. Hinman has made a similar suggestion. The procedure has also been put forward as a substitute for the Edebohl's decapsulation operation, as it is now generally believed that the success which *sometimes* follows decapsulation is due not to the removal of the capsule itself, but to the partial denervation of the kidney which decapsulation necessarily brings about.

Page and his co-workers found that renal denervation in patients with chronic nephritis caused excretion of protein to diminish in four out of five cases, while the efficiency of the kidney, as indicated by the results from the urea clearance test, showed no change, irrespective of whether the sympathectomy had been performed on one or both sides. From these results, they drew the conclusion that the operation does not increase the flow of blood to the kidney. From clinical observations of the weight and response of patients to the ingestion of water, they saw no reason to believe that denervation alters the water balance of the body, and felt justified in assuming that water-balance is not controlled by the extrinsic renal nerves. The denervated kidney "works at a higher tempo and must become fatigued much faster than the normal one which is under the regulatory influence of the central nervous system."

Renal sympathectomy cannot bring about improvement except in cases where the pain has been produced by muscular spasm. The indications for its performance are, therefore, quite limited, and the procedure should be looked upon as a last resort, when more conservative measures have failed.

Technic of Operation. This is described below.

Surgical Treatment of Arterial Hypertension

Renal sympathectomy, by means of excision of the proper nerve plexuses, has been rather widely done for the relief of arterial hypertension. Cures of the condition have not been numerous by this procedure, but many of the patients have relief of symptoms for a considerable period of time.

It was about 1930 that the first attempts to relieve arterial hypertension by such surgical procedures as celiac ganglionectomy, renal decapsulation, or even nephrectomy were made. Since then, many operative procedures have been suggested and performed, until, at present, there is an imposing array of possible interventions, only a few of which can be mentioned in any detail.

Denervation of the Kidney. In our service, we usually expose the kidney through the ordinary loin incision. The nerves that accompany the renal vessels into the hilum of the kidney are then carefully exposed and divided. In order to do this, it is necessary to dissect free the ureter and all the renal vessels. All the nerve filaments possible must be eliminated.

Smithwick's Method of Splanchnic Resection. It is the opinion of Smithwick, of the Massachusetts General Hospital, Boston, that "complete or nearly complete splanchnic resection in man should result in a characteristic change in blood pressure in every patient with hypertension. . . . If the splanchnic bed is well denervated, the blood pressure level should fall as the patient changes from the lying to the sitting and standing positions."

Technic. Originally, Smithwick divided the communicating rami of the tenth, eleventh, and twelfth dorsal segments, removing the sympathetic trunk from above the tenth dorsal to below the twelfth dorsal segment, excising as much of the great splanchnic nerve as could be reached through an eleventh rib exposure. The procedure was bilateral. The second step consisted of two stages, removing the upper three lumbar ganglia by a subdiaphragmatic extraperitoneal approach, first on one side, then on the other. Although this sometimes reduced the blood pressure satisfactorily, upon certain patients there was no noticeable effect. The procedure was then altered so that all anatomical pathways to the splanchnic bed could be reached:

Through a hockey-stick incision, the twelfth rib is resected. The upper portion of the incision is vertical, about 2 inches lateral to the midline, running up over the inner end of the eleventh rib, with the lower portion curving laterally, $\frac{1}{2}$ inch below, and parallel to, the twelfth rib. The sheaf of the sacrospinalis muscle is opened vertically to below the twelfth rib, and dissection is then carried laterally following the skin incision through the deeper structures below and beyond the tip of the rib. The twelfth rib is removed from the transverse process to the lateral border of the sacrospinalis sheath. The twelfth intercostal artery, vein, and nerve are resected over a similar area. The diaphragm is divided from its lateral border to the spine, 1 inch below, and parallel to, the pleural reflection. The pleura is then separated from the thoracic cage up to the mid-dorsal region. At this point it is possible and desirable to explore the kidney and adrenal, thereafter exposing the desired portion of the splanchnic nerve supply, which is then removed.

Usually the great splanchnic nerve is removed from its insertion in the celiac plexus upward to the midthoracic level. The celiac ganglion is not

disturbed, but care is taken to divide all branches running from the great splanchnic nerve to the aorta above the diaphragm. Interruption of the communicating rami of the ninth, tenth, eleventh, and twelfth dorsal and the first lumbar segments, together with excision of the sympathetic trunk over this area, was found to be the minimum procedure to produce a satisfactory reduction in blood pressure.

Subtotal and Total Paravertebral Sympathectomy. The technic of these procedures was reported by Grimson in 1941. It consists of a trans-thoracic and, at times, transabdominal, removal of the stellate ganglia, both thoracic chains, the celiac ganglia, and frequently the first and second lumbar ganglia. From experimental evidence this operator believes that all accessible sympathetic ganglia, including both celiac ganglia, should be removed in order to prevent restoration or regeneration of central vasomotor control. He remarks, "It is, unfortunately, not possible to determine accurately to what extent recovery of visceral vasomotor control occurs."

Contrasting this procedure with extensive splanchnicectomy: The advantages seem to be a more consistent lowering of the blood pressure, a slow, regular heart rate, a postural hypotension without tachycardia, and probably a decreased likelihood of sympathetic regeneration. The disadvantages are a greater operative morbidity and mortality, a decreased vital capacity and, in some male patients, lowering of sexual potency, sometimes prolonged weakness and postural disability, and, in general, a far more stormy convalescence.

Other Surgical Procedures. Other surgical procedures which have been reported as acting favorably upon renal hypertension are lower thoracic and upper lumbar anterior spinal nerve-root section; subdiaphragmatic splanchnicectomy, and celiac ganglionectomy.

Clinical Results of Surgery for Hypertension. Attempts to relieve hypertension by means of surgery have now been carried out for a period of nearly a dozen years, so sufficient data have accumulated to permit, some evaluation of the clinical results. At Crile's clinic in Cleveland, Ohio, and the Lahey Clinic in Boston, large series of patients have been operated upon and followed up for relatively long periods. In the latter part of 1942, Bartels, of the Lahey Clinic, made a report on 54 patients who had passed through their hands during the preceding decade, the first patient being operated upon in 1931. The first 13 patients were subjected to a supradiaphragmatic splanchnicectomy and ganglioramisectomy, while the remaining 41—regarded as a more carefully selected

group—had a two-stage subdiaphragmatic or transdiaphragmatic resection of the greater and less splanchnic nerves, with the removal of the twelfth thoracic and first and second lumbar ganglia. The adrenals and both kidneys were inspected at the same time, as recommended by Smithwick. In some cases the left kidney was decapsulated and a nephro-omentopexy carried out (provided enough omentum was available). The purpose of this was to increase the circulation of the kidney.

This series is sufficiently large to give some idea of what may be expected under average conditions. Of the earliest 13 patients operated upon, 9 had died at the time of making the report, and of the remaining 4, all had blood pressures as high as before the operation. Of the more recent cases, wherein the patients were more carefully selected and averaged considerably younger than the first group, 3 out of 41 had died, and of the remaining 38, 13 had had and maintained a satisfactory drop in blood pressure, 11 had only a slight reduction, and 14 had no change whatever after operation.

The impression gained is that age plays an important rôle in determining the benefits to be derived from surgery. Few patients over 40 years of age witnessed any permanent improvement; yet symptomatic improvement took place in 71 per cent of the entire series. The patients felt better even when the blood pressure level remained as high as before. In general, about one-third of the patients obtained a satisfactory reduction in blood pressure; but the operation is, nevertheless, well worth doing, if only for temporary symptomatic relief.

Postoperative Care Following Renal Surgery

Postoperative Care. The patient must be transported from the operating room to the bed as quickly and quietly as possible, without exposure to drafts. If the operation has been done under spinal anesthesia, his head must be kept lowered for a period of from 6 to 8 hours.

The immediate postoperative care is within the province of the nurse as a rule, and consists of careful observation of the breathing and pulse and frequent inspection of the dressings for evidence of chance hemorrhage. Signs suggesting internal hemorrhage are steady increase in the pulse rate, pallor, a drawn look, air hunger, and restlessness.

If much blood has been lost, whole blood transfusions should be given.

Fluid should be administered as soon as possible without causing nausea. If the patient does not take fluids well, they may be administered in the form of normal salt solution and 5 per cent glucose intravenously,

saline solution by hypodermoclysis, or tap water in 250 cc. doses by rectum. The fluid intake should be at least 3,000 cc. for 24 hours, and the intake and output of fluids must be carefully measured and charted (see p. 1154).

Nephrostomy and pyelostomy tubes must be inspected frequently to see that they drain freely and do not become kinked, and the drainage must be carefully charted. Irrigations are often given by the doctor, in order to keep the wound open and draining freely.

Sedative medication is usually given for the first 2 or 3 days: morphine, 0.01 Gm. every 4 hours for 2 doses, then codeine, 0.06 Gm. every 4 hours for the next 48 hours or longer, as required to control pain and restlessness.

Hot, clear fluids are usually given the first postoperative day (unless there is nausea); hot fluids supplemented by milk, fruit juices, and gingerale the second day; a soft diet the third day, and a regular diet the sixth day. After the first week a special diet is usually unnecessary except in cases of renal tuberculosis with bladder involvement (see p. 1193), and in stone cases, in which the high vitamin acid ash or alkaline ash diet for urinary stone is given, depending upon the composition of the stone (p. 1189). In nephropexy cases, a high caloric diet is advisable for underweight patients; otherwise the patient is given a regular diet supplemented by vitamin intake.

Postoperative Complications. *Hemorrhage* is the chief danger following renal surgery. The probability of postoperative hemorrhage following nephrectomy is rather remote if the pedicle has been properly ligated after clamping, but at times even the most competent surgeon may not be able to avoid this complication. Formerly, when our kidney incisions were repaired by means of mattress sutures, secondary hemorrhage frequently occurred, due to the plug of resulting necrotic tissue separating and exposing sizable vessels. Our newer method of closing kidney wounds, with fat fixed in place by ribbon gut, has reduced the incidence of hemorrhage following nephrotomy and heminephrectomy to a minimum. Hemorrhage may occur several days after operation, and these remote hemorrhages are most serious. A careful watch must, therefore, be kept for signs of such an occurrence even when all danger appears to be past. Hemorrhage will be manifested by (1) symptoms of shock, such as pallor, a steady increase in the pulse rate, a drop in blood pressure, air hunger, and restlessness, and (2) the appearance of bright red blood on the dressing, which must be frequently inspected.

Embolism is less common following renal surgery than after pelvic surgery, but occurs with sufficient frequency to be feared. It manifests itself by disturbed respiration, increased pulse rate, unconsciousness, cold clammy skin, and other evidences of extreme shock.

Infarct of the kidney results from the sudden plugging of a small or large terminal artery in the renal cortex. It is accompanied by pain and hematuria.

Pneumothorax, due to puncture of the pleura in extensive renal surgery, may cause great distress. It is relieved almost instantly by withdrawing the air from the pleura by means of a syringe and a needle fitted with a two-way stop-cock.

Vomiting rarely occurs when spinal anesthesia is used. It may be due to other factors than anesthesia, however. When it is troublesome and persistent, the stomach should be lavaged with a 2 per cent solution of sodium bicarbonate, and chloretone in 3-grain doses administered. Following gastric lavage it may be advisable to employ the Wangenstein suction or the Miller-Abbott suction tube in order to remove gas and fluid from the gastrointestinal tract and prevent obstruction.

Hiccough is often a manifestation of approaching uremia, and may be very persistent. Gastric lavage with weak sodium carbonate solution will usually relieve the condition. When it is very obstinate, inhalations of carbon dioxide and oxygen will frequently be helpful.

Postoperative Follow-up. All patients who have had surgery of the kidney should be required to report for follow-up examination and such treatment as may be necessary. In certain conditions, such as tuberculosis and stone, the surgeon's work has only just begun when he allows the patient to leave the hospital.

B. NON-OPERATIVE TREATMENT OF THE KIDNEY

Most of the non-operative methods of treating pathological conditions of the kidney have been considered elsewhere in this book. The reader is referred to the following sections: Chemotherapy (p. 1162), Urinary Antiseptics (p. 1177), Diet (p. 1187), Treatment of Inoperable and Post-operative Urogenital Tuberculosis (p. 1196), and Radium and Roentgen Therapy of Tumors of the Kidney and Ureter (p. 1758).

Ureteral Catheterization and Lavage of the Renal Pelvis

Ureteral catheterization and pelvic lavage is indicated in the treatment of many subacute and chronic renal infections. If, however, the pyelo-

nephritis is of long standing, so that destruction of the renal parenchyma has already taken place, lavage of the pelvis will be of little value. As a preparation for operation for hydronephrosis, or the removal of stone from a kidney known to be infected, pelvic irrigation is of service in rendering the field more aseptic.

The beneficial effects are probably due more to the opening up of the ureter by the passage of the catheter than to the direct action of the antiseptic solution employed, although the latter is likely to receive the credit.

Renal pelvic lavage is, of course, a cystoscopic procedure unless an indwelling catheter or nephrostomy tube is being used. The eye of the catheter should be passed completely to the pelvis, if possible. A syringe of 20-cc. capacity is suitable for pelvic lavage. From 5 to 10 cc. of the irrigating solution may be injected at a time, with intervals between each filling of the pelvis, to permit the fluid to escape.

Suitable solutions for lavage of the renal pelvis are: silver nitrate, in strengths varying from 1:1,000 to 1:5,000; acriflavine, 1:2,000; rivanol dextrose, 1:2,000; phosphoric acid, 1:1,500, and aluminum acetate, 0.25 per cent. Various citrate solutions are used for dissolvable stones (see p. 1617).

Indwelling Ureteral Catheterization

The indwelling ureteral catheter is a valuable aid in the treatment of hydronephrosis, renal infections, and stone. A patient whose condition at first makes any operation impossible may sometimes be tided over until he can be built up physically and become a relatively good operative risk.

An excellent example of the type of lesion that is frequently benefited by this mode of treatment is the pyelonephritis of pregnancy. Urologists are unanimous as to the value of indwelling ureteral catheterization in the treatment of this common condition, but there is considerable disagreement regarding the size of the catheters to be used. The ureters being dilated during pregnancy, two rather large catheters (No. 8 or 9 F.) should be inserted through the cystoscope and left in place, being fixed to the patient's thighs with adhesive tape. This permits proper drainage from the affected kidneys and relieves the toxicity and discomfort accompanying pregnancy pyelonephritis.

The indwelling ureteral catheter is also a most valuable adjunct in the treatment of the pyelitis of infancy and childhood.

Indwelling ureteral catheters are usually removed within a short period (less than 24 hours) or else they are left in place for at least 4 or 5 days. If they are removed sooner, the edema which always follows the traumatization of catheterization may block up the ureteropelvic outlet tighter than before, and cause considerable difficulty, not the least of which would be the reinsertion of the catheters. However, the larger catheters should not be allowed to remain in position too long, because there is always danger of the formation of encrustations if the urine is not kept acid, as well as danger of pressure necrosis, as was proved by E. Clay Shaw in his experiments on dogs.

The catheters should be frequently observed to see that they are draining satisfactorily. Should they show a tendency to become blocked, irrigation with saline or one of the usual antiseptic solutions should immediately be instituted.

Dilatation of the Ureter

Dilatation of the ureter, with bougies and catheters, produces good drainage. In cases of hydronephrosis due to stricture of the ureter, dilatation should be done at frequent intervals until there is no evidence of back pressure. Ureteral catheters of increasing size, up to No. 9 or 10 F., should be used, the renal pelvis being irrigated at the end of the dilatation period. If the hydronephrosis is not too extensive, the establishment and maintenance of good drainage is frequently the only treatment required.

In chronic or recurrent pyelonephritis, in both children and adults, search should always be made for stricture or other factors causing obstruction of the ureter, since permanent cure of the renal infection is impossible so long as there is obstruction to the urinary outflow. Stricture at the ureteropelvic junction usually requires surgical intervention, but stricture elsewhere in the duct is amenable to dilatation as a rule.

Small, non-impacted calculi, obstructing the urinary outflow, can be made to pass by dilatation of the ureter below the obstructing mass in the majority of instances.

Forcing of Fluids

In addition to the establishment of free drainage, every effort should be made to irrigate infected kidneys by the forcing of fluids. When fluids are being forced, the blood findings should be frequently checked and the urinary output carefully estimated (Forcing of Fluids, Chart-

ing Fluid Intake and Output, p. 1154). The forcing of fluids is unwise with patients who have any form of heart disease; but, barring cardiac complications, there is practically no limit to the amount of fluid which may be taken with benefit to the renal condition.

Bacteriophage in the Treatment of Urinary Infections

The existence, in the animal body infected with disease-producing bacteria, of an antagonistic living property which, under favorable conditions, can bring about lysis of the causal organisms was first made known by Twort and d'Herelle (working independently) in 1915 and 1916. To this disintegration of bacteria by filter-passing lysins, which multiply as they destroy the bacterial host, d'Herelle applied the term *bacteriophagy*.

Bacteriophage therapy has been successful in a fair percentage of urinary-tract infections. The introduction of sulfanilamide, however, has materially lessened its usage in urology.

As pointed out by Wehrbein, the bacteriophage, to be effective, must be brought in massive direct contact with the infecting organisms; therefore, this form of therapy is likely to be successful only in relatively superficial infections, such as cystitis and pyelitis. In renal abscesses and infections of the prostate or seminal vesicles, cure cannot be expected unless the suspension can be injected directly into the site of inflammation. It may be administered subcutaneously or intravenously, but, thus given, the response is much slower and the results not nearly so favorable as in direct bacteriophage therapy.

The most important step in bacteriophage therapy is the preparation of the "phage." It is absolutely necessary to obtain a pure culture. The strain of infecting organism must be determined, and a bacteriophage with a specific and highly potent lytic action for the respective strain must be prepared. The bacteriophage should be capable of causing permanent lysis of all the causal organisms within 24 to 48 hours. A bacteriophage of low potency is not only temporary in its beneficial effects but eventually results in a secondary culture of bacteriophage-resistant organisms, thus doing more harm than good.

The most common source of bacteriophage for the colon bacillus and allied groups is sewer water and the stools of patients having chronic colitis. The best source of "phage" for coccal infections is the pus from carbuncles or furuncles, or cases of chronic osteomyelitis or peritonitis.

For the preparation of "phage," the reader is referred to the excellent article on *Bacteriophage in the Treatment of Urinary Infections*, by H. L. Wehrbein, with an appendix on the *Technique of Phage Preparation*, by Louis Nerb, in the *American Journal of Surgery*, July, 1935.

The bacteriophage may be administered in a number of ways. It may be given orally, or injected intravenously or subcutaneously. In employing the bacteriophage in the urinary tract, the solution is commonly injected directly into the renal pelvis or bladder.

The proliferation of bacteriophage is facilitated in an alkaline medium.

Wehrbein's experience with the technic of bacteriophage administration led him to emphasize the following points:

1. The bacteriophage must be absolutely and quickly effective before it is used. It should lyse a billion microorganisms per cubic centimeter in 3 to 5 hours. Prolonged incubation should show no second growth.

2. The bacteriophage should be placed in as large a quantity and in as concentrated a form as possible in the infected area. If the kidney pelvis is infected, the pelvis should be actually filled with the "phage" solution, using a large catheter. If the bladder only is infected, at least 50 cc. should be placed in the empty bladder. All antiseptics must be avoided.

3. If the first application of the bacteriophage is unsuccessful, it is useless to repeat.

The most striking results with bacteriophage have been achieved in acute urinary infections due to the colon bacillus. The securing of a sufficiently potent bacteriophage for these organisms is relatively easy. An effective bacteriophage, brought in direct contact with the causal organisms, is likely to be rapidly successful in these cases. The chronically infected case is a much more difficult problem, due to the difficulty of preparing efficient bacteriophages. The existence of a symbiosis between the infecting organism and a weak bacteriophage prevents satisfactory response to treatment in these cases. Mixed infections are common, and the process of securing the bacteriophage is complicated by the necessity of providing lysins for a number of different organisms. In coccal urinary infections the results with bacteriophage have not, on the whole, been very successful.

BIBLIOGRAPHY

- ABBOTT, A. C., AND STEPHENSON, EARL: Renal sympathectomy. *J. Canad. M. A.*, 39: 542, 1938.
- ADSON, A. W.: Indications for operation on the sympathetic nervous system. *J. A. M. A.* 106: 360, 1936.

- BARNES, R. W., AND BERGMAN, R. T.: Transperitoneal nephrectomy. *J. Urol.*, 46: 545, 1941.
- BARTELS, E. C., *et al.*: Surgical treatment of hypertension (results in 54 cases). *Ann. Int. Med.*, 17: 807, 1942.
- BEER, E., *et al.*: Heminephrectomy in disease of double kidney; 14 cases. *Ann. Surg.*, 108: 705, 1938.
- BILLINGTON, WILLIAM: The therapeutic value of nephropexy. *Brit. M. J.*, 2: 975, 1928.
- BOYD, M. L.: Indications for nephrostomy and nephrectomy. *J. A. M. A.*, 99: No. 15, 1932.
- BRAASCH, W. F., AND PRIESTLEY, J. T.: Late results in conservative management of nephrolithiasis. *J. A. M. A.*, 109: 1703, 1937.
- BRUGER, M., AND CARTER, R. F.: Nephro-omentopexy and nephromyopexy in the treatment of hypertension. *Ann. Surg.*, 113: 38, 1941.
- CABOT, HUGH, AND HOLLAND, W. W.: Nephrostomy: indications and technique. *Trans. Am. Assoc. Genito-Urin. Surg.*, 24: 95, 1931.
- CALDWELL, J. A.: Bacteriophagy in urinary infections following the administration of the bacteriophage therapeutically. *Arch. Int. Med.*, 41: 189, 1928.
- CAMPBELL, M. F.: Resection of the kidney. *J. A. M. A.*, 117: 1223, 1941.
- CORCORAN, A. C., AND PAGE, I. H.: Renal blood flow and sympathectomy in hypertension. *Arch. Surg.*, 42: 1072, 1941.
- CRILE, GEORGE, AND CRILE, GEORGE, JR.: Blood pressure changes in essential hypertension after excision of the celiac ganglion and denervation of the aortic plexus. *Cleveland Clin. Quart.*, 3: 268, 1936.
- DALSACE, R.: Applications du bacteriophage de d'Herelle à la cure des infections urinaires. *J. d'urolog.*, 21: 123, 1926.
- DAVIS, DAVID M.: Resection of the kidney. *Am. J. Surg.*, 12: 272, 1931.
- DEVRIES, JOHN K.: Hypemephroma, papilloma, and stone occurring in horseshoe kidney. *Am. J. Surg.*, 10: 487, 1930.
- DEMING, CLYDE L.: Renal circulation following various types of nephrostomies. *Am. J. Surg.*, 4: 424, 1928.
- DEMING, CLYDE L.: Nephroptosis, causes, relation to other viscera, and correction by a new operation. *J. A. M. A.*, 95: 251, 1930. Also: *Am. J. Surg.*, 9: 218, 1930.
- EISENDRAH, D. N.: The relation of variations in the renal vessels to pyelotomy and nephrectomy. *Ann. Surg.*, 71: 726, 1920.
- FINDLEY, T., *et al.*: Effects of sympathectomy on renal blood flow in essential hypertension. *Surgery*, 12: 64, 1942.
- FLANDRIN, P.: L'énervation renale. *Arch. urol. de Necker*, 4: 101, No. 2, 1923-5.
- GIBSON, T. E.: The present status of renal sympathectomy. *J. Urol.*, 36: 334, 1936.
- GOLDSTEIN, ALBERT E.: New surgical procedure for the treatment of polycystic kidneys. *J. Urol.*, 34: 536, 1935.
- GOLDSTEIN, ALBERT E.: Accidents in renal surgery. *Surg. Gynec. & Obst.*, 65: 515, 1937.
- GRABER, W. J., AND KNOEFF, L.: Surgical management of renal and ureteral calculi. *Urol. & Cutan. Rev.*, 44: 442, 1940.
- GRIMSON, K. S.: The sympathetic nervous system in neurogenic and renal hypertension. *Arch. Surg.*, 43: 284, 1941.
- GRIMSON, K. S.: Total thoracic and partial total lumbar sympathectomy and celiac ganglionectomy in the treatment of hypertension. *Ann. Surg.*, 114: 753, 1941.
- GRIMSON, K. S.: The surgical treatment of hypertension. *Internat. Abst. Surg.*, 75: 421, 1942.
- GUTIERREZ, ROBERT: The clinical management of the horseshoe kidney. *N. Y., P. B. Hoeber*, 1934. Also, *Am. J. Surg.*, 14: 657, 1931.

- HARRIS, S. H.: Renal sympathectomy and renal sympatheticotony; the scope and limitations of the operation. *Lancet*, 1: 424, 1935.
- HARRIS, S. H., AND HARRIS, R. G. S.: Renal sympathetico-tonus; renal pain and renal sympathectomy. *Brit. J. Urol.*, 2: 367, 1930.
- HARRIS, S. H., AND HARRIS, R. G. S.: Renal sympathetico-tonus and renal sympathectomy. *J. Canad. M. A.*, 24: 235, 1931.
- HENLINE, R. B.: Fibrosarcoma of a polycystic kidney with extension into the vena cava: case, with surgical removal.
- HERBST, W. P.: Normal and abnormal motility syndromes of the upper urinary tract, with indications for drug and sympathectomy therapy. *Minnesota Med.*, 15: 413, 1932.
- HERBST, W. P.: Pyeloscopy and urographic study, before and after renal sympathectomy. *J. A. M. A.*, 99: 2003, 1932.
- HESS, ELMER: Renal sympathectomy. *Penn. M. J.*, 33: 741, 1930.
- HESS, ELMER: Renal sympathectomy. *Internat. Clinics*, 4: 28, 1931.
- HESS, ELMER: Nephrotomy; its indications, limitations, and terminal results. *Calif. and West. Med*, 41: 74, 1934.
- HESS, ELMER: Heminephrectomy, its indications and limitations. *J. Urol.*, 38: 43, 1937.
- HESS, ELMER: The management of the nephroptotic patient. *Urol. & Cutan. Rev*, 42: 703, 1938.
- HIGGINS, C. C., AND GLAZIER, M.: Relative merits of the scalpel and high-frequency current in nephrostomy. *Surgery*, 9: 220, 1941.
- HOLMES, ROY J., AND COPLAN, M. M.: Conservative renal surgery. *J. Florida M. Assoc.*, October 1931.
- KINDALL, L. E.: Conservative surgery, with special reference to kidney wounds. *Calif. & West Med*, 49: 115, 1938.
- KIRWIN, THOMAS J.: Calcified renal cyst. *J. Urol.*, 15: 273, 1926.
- KOLISCHER, G., AND JONES, A. E.: Surgical intervention in medical kidney diseases. *Illinois M. J.*, 49: 215, 1926.
- KOLL, IRVING S.: The transplantation of fat in prostatic and kidney surgery. *J. A. M. A.*, 68: 536, 1917.
- KRUEGER, A. P., *et al*: Observations on the bacteriophage in infections of the urinary tract. *J. Urol.*, 23: 427, 1930.
- LARKUM, N. W.: Bacteriophagy in urinary infections. *J. Bacteriol.*, 12: 203, 1926.
- LAZARUS, J. A.: Indications for surgery in polycystic kidneys. *Urol. & Cutan. Rev.*, 38: 457, 1934.
- LECOMTE, R. M.: The management of renal tumors, including cysts. *J. A. M. A.*, 105: 1963, 1935.
- LECOMTE, R. M.: Symptoms, diagnosis, and treatment of renal cysts. *Southern M. J.*, 31: 632, 1938.
- LIVERMORE, GEORGE R.: Nephrostomy: cases. *Trans. Am. Assoc. Genito-Urin. Surg.*, p. 367, 1933.
- LOWSLEY, O. S.: Some new developments in renal surgery. *Southern M. J.*, 27: 139, 1934.
- LOWSLEY, O. S.: Anomalies of the kidney and movable kidney. *Dean Lewis' Practice of Surgery*, Vol. VIII. Hagerstown, Md., W. F. Prior Co., Inc., 1935.
- LOWSLEY, O. S.: Experimental surgery of the kidney. *J. Kansas Med. Soc.*, 36: 397, 1935.
- LOWSLEY, O. S.: Advances in renal surgery, with particular reference to nephropexy. *J. Missouri State Med. Assoc.*, 32: 313, 1935.
- LOWSLEY, O. S.: Modern renal surgery, with particular reference to heminephrectomy. *N. Y. State J. Med.*, 36: 591, 1936.
- LOWSLEY, O. S.: Further experiences with a new principle in renal surgery. *Penn. M. J.*, 41: 345, 1938.

- LOWSLEY, O. S., AND BISHOP, C. C.: A new method of repairing kidney wounds. *Surg. Gynec. & Obst.*, 57: 494, 1933.
- LOWSLEY, O. S., AND HUNT, R. W.: Plastic operations in urologic surgery. *Southern M. J.*, 35: 676, 1942.
- LOWSLEY, O. S., KINGERY, L. B., AND CLARKE, H. C.: Surgical significance of certain abnormalities of the urinary tract. *J. Urol.*, 11: 293, 1924.
- LOWSLEY, O. S., AND KIRWIN, T. J.: *Text-book of Urology*, pp. 659-679. Phila., Lea & Febiger, 1926.
- LUND, F. B.: *Rovsing's operation for congenital cystic kidney*. *J. A. M. A.*, 63: 1083, 1914.
- MACNEAL, W. J., *et al.*: Use of bacteriophages in the treatment of colon bacillus infections of the urinary tract. *Arch. Surg.*, 29: 633, 1934.
- MATHÉ, C. P.: Movable kidney. *Surg. Gynec. & Obst.*, 40: 605, 1925.
- MATHÉ, C. P.: Renal surgery: its pitfalls and complications. *Calif. & West. Med.*, 28: 57, 1928.
- MATHÉ, C. P.: Nephropexy: present-day status and description of new technique. *Surg. Gynec. & Obst.*, 57: 538, 1933.
- MELEN, D. R.: Nephropexy by means of a fascial hammock. *J. A. M. A.*, 100: 1167, 1933.
- O'CONOR, V. J.: Value of nephrostomy, ureterolysis and nephropexy in selected cases. *J. A. M. A.*, 93: 1114, 1929.
- O'CONOR, V. J.: Resection of large solitary renal cysts; description of a satisfactory technique. *J. Urol.*, 35: 561, 1936.
- PAGE, S. H.: Effect of renal denervation on patients suffering from nephritis. *J. Clin. Invest.*, 14: 1443, 1935.
- PAPIN, E.: Indications et technique de la nephropexie. *Paris chir.*, 20: 1, 1928.
- PAPIN, E., AND AMBARD, L.: Resection of nerves of kidney for nephralgia and small hydronephrosis. *J. Urol.*, 11: 337, 1924.
- PRIESTLEY, J. T., AND SCHULTE, T. L.: Preoperative and postoperative care for patients who have operations on the kidney. *Surg. Clinics of North Am.*, 20: 1049, 1940.
- QUINBY, W. C.: Transperitoneal approach to the kidney; its indications and limitations. *J. Urol.*, 6: 135, 1921.
- QUINBY, W. C.: A note on the results of decapsulation of the kidney for various forms of nephritis. *J. Urol.*, 13: 321, 1925.
- QUINBY, W. C.: Factors influencing the operative procedure in hydronephrosis. *J. A. M. A.*, 93: 1709, 1929.
- RATHBUN, N. P.: Some of the accidents of renal surgery. *J. Urol.*, 20: 427, 1928.
- RAYCH, A.: Multilocular tuberculous cyst of the kidney; resection and recovery. *J. Urol.*, 25: 223, 1931.
- RITTER, J. S.: Nephro-omentopexy for the relief of hypertension. *J. Internat. Coll. Surgeons* 4: 25, 1941.
- ROVSING, THORKILD: My technique in operations on the kidney. *Practitioner*, 118: 164, 1927.
- ROSS, J. C.: Decapsulation and denervation of the kidney. *Liverpool Med. Chir. J.*, 46 (Pt. I): 78, 1938.
- RUMPEL, O.: Nierenresektion bei einseitiger Langmiere (gekreuzte Dystopie). *Zentralb. f. Chir.*, 59: 1290, 1932.
- SCHULTZ, E. W.: Bacteriophage as a therapeutic agent in genito-urinary infections. *Calif. & West. Med.*, 36: 33 and 91, 1932.
- STONE, L.: Heminephrectomy. *J. Urol.*, 28: 301, 1932.
- STRODE, J. E.: *Kidney suspension by the use of fascia lata*. *J. Urol.*, 32: 171, 1934.
- TWINEM, F. P.: The surgical management of bilateral nephrolithiasis. *Am. J. Surg.*, 24: 124, 1934.

- TWINEM, F. P.: Polycystic kidneys with bilateral perinephric abscesses. bilateral operation. J. A. M. A., 106: 206, 1936.
- TWINEM, F. P.: Prevention of recurrent renal stone by calyceal resection. Surg. Clinics North Am., 20: 299, 1940
- VON LICHTENBERG, A.: Plastic surgery of the renal pelvis and ureter. J. A. M. A., 93: 1706, 1929.
- WALTERS, W.: Resection of the kidney pelvis for hydronephrosis; its complications and results. Surg. Gynec. & Obst., 51: 711, 1930.
- WALTERS, W., AND BRAASCH, W. F.: Surgical aspects of polycystic kidneys. Report of 85 surgical cases (31 nephrectomies). Surg. Gynec. & Obst., 58: 647, 1934
- WEHRBEIN, H. L.: Bacteriophage in the treatment of urinary infections. with an appendix on the technique of phage preparation (by Louis Nerb). Am. J. Surg., 29: 48, 1935
- WESSON, M. L.: Treatment of traumatic rupture of the kidney. Ann. Surg., 83: 234, 1926.
- WHITMORE, E. R.: Hypernephroid tumors of the kidney. Southern. M. J., 29: 1051, 1936.
- WOODS, W. W.: Surgical treatment of hypertension (splanchnicectomy and sympathectomy). J. Urol., 48: 16, 1942
- WRIGHT, B. W.: Heminephrectomy, report of 3 cases. Urol. & Cutan. Rev., 36: 592, 1932
- YOUNG, H. H., AND DAVIS, E. G.: Double ureter and kidney with calculous pyonephrosis of one half; cure by resection, the embryology and surgery of double ureter and kidney. J. Urol., 1: 17, 1917.
- YUNCK, W. P., AND FORSYTHE, W. E., JR.: Calyceal resection: report of clinical and experimental cases. J. Urol., 46: 396, 1941.

CHAPTER XXXIX

RADIUM AND ROENTGEN-RAY THERAPY OF THE GENITO-URINARY TRACT

INTRODUCTION

Although radiation has been at the disposal of therapists for more than three decades, there is little unanimity regarding its usefulness or the best methods of applying it. The rapidly growing literature is decidedly controversial. Recognized authorities hold completely opposing views upon the management of the various clinical manifestations of cancer. This perplexity is chiefly due to (1) our incomplete understanding of cancer and (2) our uncertain knowledge of the action of x-rays and radium.

In urology, radiation has a wide application, particularly in the treatment of malignant tumors of the bladder, prostate, and testicle. Every urologist should therefore be familiar with the relation and similarities of the rays produced by x-ray and radium, the manner of distribution and measurement of radiant energy, and the terminology of radiation therapy. Most important of all is the ability to judge, from clinical and microscopic study, the particular forms of cancer in which radiation is desirable or imperative. This involves an appreciation of its limitations and contraindications quite as much as a knowledge of how to use it to the greatest advantage. On these points there are at present wide differences of opinion, creating a situation that is highly confusing to the general practitioner and the specialist alike.

Discovery of the Roentgen Rays and Radium. In 1895 Konrad Roentgen discovered that by arresting the particles in the discharge produced by passing an electric current through a vacuum tube, a light ray, invisible to the eye yet capable of passing through most opaque objects, could be produced. This discovery—now known as the x-ray or roentgen ray—incited many other scientists to search for substances which, under suitable conditions, would produce similar rays. These researches eventually led to the demonstration of the principle of radioactivity, which was proved to be an attribute of the element uranium and all its compounds. In experimenting with uranium, Professor and

Madame Curie discovered and isolated radium. It was not until 1903, however, that Rutherford and Soddy advanced the theory of atomic disintegration, the confirmation of which made possible the modern therapeutic employment of radium.

Atomic Disintegration. Radioactivity is induced by disintegration of the atoms of which the radioactive substance is composed, but what causes this disintegration science cannot explain. The disintegration can be neither arrested nor controlled, but goes steadily forward, affecting certain atoms when they reach a certain stage of development. In any given quantity of radioactive material a definite proportion of its atoms are always breaking up, emitting radioactivity as they do so. Thus, spontaneous liberation of energy is constantly going on, and it is probable that this process is infinitely wider than science has even dreamed.

Types of Rays. Three types of rays emitted by radioactive material have been identified. These have been designated as alpha, beta, and gamma rays.

Alpha rays are positively charged helium atoms, having a velocity about one-tenth that of light. Though their ionizing power is great, their powers of penetration are weak—so frail a substance as a sheet of paper serving to divert them.

Beta rays are tiny particles of negative electricity, usually designated as electrons. They are closely allied to the cathode rays from which Roentgen derived the x-rays, and were first observed by Giessel in 1899. Lighter than alpha particles, the beta rays vary in their penetrating power, as well as in their velocity. When they travel at approximately the speed of light, they possess considerable penetrating power, but can be diverted by the intervention of certain metallic substances, such as gold, silver, and platinum.

Gamma rays are not atomic particles, but high-frequency vibrations in the ether, closely analogous to x-rays. Like light and all other forms of radiation, the gamma rays are electromagnetic disturbances of the ether, having a periodic variation in time and space.

Wave-length depends upon the rapidity with which these vibrations follow one another. When the succession is very rapid, the wave is *short*; if the vibrations are slower in recurring, the wave-length is designated as *long*. There are, of course, an infinite number of intervening gradations, but in therapeutic and mechanical employment these fine distinctions are disregarded.

It is the gamma ray that is utilized in medicine. The alpha rays are

never employed and the beta rays only occasionally. The penetrative powers of the gamma ray are greater than those of the alpha and beta rays. These powers depend upon the wave-length, which is very short—even shorter than that of the x-ray which is used in therapy. Whether the difference in clinical effects produced by gamma rays and x-rays is due only to the difference in wave-lengths, penetration, and absorption, or whether there is a difference in the biological effects, has not been established. Gamma radiation is especially penetrating through substances that are opaque to light. This is important to remember when considering the medical applications of radioactivity.

The chemical properties of radioactive materials, the time periods at which they undergo atomic changes, and their powers of emitting radiation differ greatly from one substance to another. The speed and degree of penetrative power possessed by the rays from a radioactive material depend upon the type of atoms which are ejecting the rays. Radium emits alpha radiation alone, but as its products accumulate, its activity is developed. Though it continuously produces other forms of radioactivity, it is now possible to separate the radium itself from its products. Any given amount of radium will produce its emanation in the form of the gas *radon* at a given rate, irrespective of whether the radon be separated from its parent radium or not.

Radon. Radon is an inert gas belonging to the argon order of gases. The heavy molecules of which it is composed are single atoms and are unable to combine with any others. Radon is produced commercially by dissolving radium salts in hydrochloric acid, sealing the container, and then pumping off, at stated intervals, the emanation which collects in the tube. It is this emanation—not the radium itself—which is of therapeutic value. When radium element is used medicinally, the salt is placed in a tube, in which radon collects, and it is from this emanation that the therapeutic gamma radiation is given off.

The advantages of using a compressible gas instead of a heavy salt, when it must be fitted into containers used for application to all parts of the human body, are obvious. The chief drawback to the use of emanation alone, instead of allowing the element to produce the emanation in a tube placed directly at the site of the lesion to be treated, is that radon does not remain stable. As soon as the emanation reaches its maximum intensity (which takes about 2 hours), it begins to decline, losing one-half its radioactivity every 3.85 days. In the presence of the mother element, the radon is continuously renewed, so that the activity

is practically constant; but a tube containing only the emanation will decline steadily in activity until finally it becomes wholly inert. This very drawback, however, has also certain advantages. Because the rate of decay is precisely known, it can be accurately measured to deliver a given amount of radiation during the time that its radioactivity steadily declines.

Radium is enormously expensive, but the cost of its emanation, radon, amounts only to the expense of putting the radium into solution and withdrawing the gas into suitable containers, plus the cost of the containers themselves and the expense attendant upon merchandising. Radon may be shipped considerable distances from the place where the radium is held in solution, so that the same amount of radium which would be needed to treat a comparatively few patients, if it had to be placed in individual containers, can be made to work 24 hours a day producing gas to fill these individual containers. In this way hundreds may be treated instead of the few who could be served by the radium itself.

Measurement of Radium and Its Emanation. In 1912 a tube of pure radium chloride, containing 21.99 mgm., which had been especially prepared by Madame Curie herself, was accepted as an international radium standard of measurement. The weight of quantities of radium put up for clinical purposes is generally expressed in grams and milligrams. The gas radon is, therefore, derived from salts of known weight, and its quantity must bear a certain relation to the quantity of radium from which it was obtained. In 1910 the International Congress of Radiology decided upon a unit of measurement for radon which they termed a *curie*, in honor of radium's discoverer. One curie is the amount of radon in equilibrium with 1 gm. of radium element. The sub-units, *millicurie* and *microcurie*, respectively correspond to 1 mgm. and 1 one-thousandth part of a milligram of radium. In clinical practice the contents of a container of radon is usually measured in millicuries.

The clinical use of radon is limited by the rate of decay of the gas. Thus, if a tube containing 100 millicuries of radon at its highest intensity is placed in contact with a malignant lesion and allowed to remain 1 day, its value will have decreased to 83.5 millicuries. If left for 2 days, the value will be only 69.7 millicuries; for 3 days, 58.2 millicuries; for 6 days, 33.9 millicuries. At the close of the tenth day only 16.5 millicuries will remain in the container. In the interstitial method of application, which is that most used with radon, the decay rate is calculated and a small tube or seed is inserted and left permanently in the tissues to be treated,

for at the end of a given period it will entirely have lost its radioactive properties.

Radium Containers. In using radium element, the therapist is somewhat limited as to the type of container; but when radon is employed, it can be compressed into any shape of container the human mind can devise. As, except in rare instances, only the therapeutic gamma rays are employed, it is necessary that the containers be of a material which will effectively screen out the undesirable alpha and beta rays. The alpha rays are easily eliminated, but the far greater penetrative powers of the beta rays make them more difficult to control. Rubber and glass are frequently used, but they must be combined with some metal in order to be effective. It is customary to employ either gold or platinum for most of the work. A very thin sheet of either will effectively cut off the caustic beta rays and prevent burning of the tissues.

Measurement of X-Ray Dosage. There are several ways of measuring x-ray dosage. Since 1928, when it was adopted by the International Congress of Radiology, at Stockholm, the ionization method has been the accepted standard. But the unit skin dose (U.S.D.), as determined by the pastille method, is still extensively used, so that the urologist should understand both methods.

International "R" (roentgen) Unit. If air is subjected to an x-ray beam, it will become ionized—that is, the molecules of which it is composed will be split up into positively and negatively charged particles. If two bodies of opposing electrical sign are contained in air so affected, the charged particles which result from the splitting up of the molecules will display electrical attraction for the body of opposite sign to themselves. This will cause a current to flow from one body to the other; but if the charge which split up the molecules is not strong, before they can reach the opposite body they will be re-attracted to their own sign and re-combined. Therefore, unless the charge affecting the two bodies is sufficient to offset such re-combination, there can be no continuous current. The fact that the current is established indicates that the two bodies are at a potential sufficient to prevent re-combination. This charge is designated as *saturation voltage*.

The device for measurement is an enclosed chamber the two sides of which are oppositely charged. When the roentgen-ray is thrown upon the air imprisoned in this chamber, and held there under measured temperature and pressure, it is possible to measure the amount of current which ionization can produce in a given time in a known quantity of air.

This was designated by the Stockholm Congress as the international "r" unit, which is defined as "that quantity of radiation which, where the secondary electrons are fully utilized, and in the absence of wall effect in the ionization chamber, produces in 1 cc. of air at standard temperature and pressure a degree of ionization sufficient to permit the passage of one electrostatic unit of charge between points at saturation potential."

Unit Skin Dose. After the acceptance of the standard "r" unit, it was generally employed for scientific purposes; but in the clinical practice of x-ray diagnosis and therapy the formerly employed unit skin dose is still too useful to be abandoned. As it is a biological unit, it can never be entirely accurate, for it must be varied according to the nature of the skin of the person exposed to radiation, as well as apportioned to his age and systemic condition. However, the experienced radiologist who thinks in terms of the skin unit is unlikely to give his patient an overdose, and will have no difficulty in adjusting this biological conception to the chemical and physical units.

The unit skin dose, or erythema dose, will vary considerably with the individual opinion of the therapist as to what constitutes an "erythema." This may be all the way from a faint reddening of the skin to the actual production of a first-degree burn. It will vary also with the part of the patient's body which is exposed to the rays. For example, an erythema dose to the inside of the thigh would be much less than one to the back of the hand of the same person. The unit skin dose may, therefore, be defined as "that quantity of radiation which, when brought into contact with normal abdominal skin of a healthy adult, in a single exposure, lasting from one-half hour to a full hour, will produce a bright red erythema in from 6 to 21 days, followed by pigmentation and desquamation (Portmann)."

Effects of Radiation. The factors deciding the success or failure of radiation treatment are the penetrative and absorptive powers of the rays and the response of the living cells.

Devitalization of the neoplastic cells is the end sought when applying radiation. The exact mechanism by which the death of the cell takes place is unknown. The immediate effect of radiating such a cell appears, microscopically, as an alteration in the nucleus and certain changes in the protoplasm manifested by alterations in the shape and size of the cell. Clinically, the effect is evidenced by regression of the tumor mass.

Though radiation is directed toward the neoplastic cells, its effect is also felt upon the blood vessels and connective tissue by which these

cells are supported. Such effects are edema, anemia, decreased resistance to infection, and, finally, necrosis and sloughing. The ideal of radiation therapy is to devitalize the malignant cells while at the same time avoiding devitalization of the surrounding normal tissues, as well as the formation of dense fibrosis.

Caustic irradiation destroys all tissue, both normal and neoplastic within the radius of its action. It is distributed by insufficiently filtered radioactive centers. *Selective irradiation* attempts to devitalize the neoplastic cells while respecting the normal supporting tissues. It is made possible by the screening out of caustic rays by means of filters of gold, platinum, or baser metals, and by the utilization of variations in radiosensitivity of different tissues.

Radiosensitivity. If the radiosensitivity of a given tumor could be accurately predicted, the selection of the best treatment for the lesion in question—whether surgery or irradiation alone or in combination—would be relatively simple. However, although radiosensitivity has been intensively studied, this complex phenomenon remains unexplained. Our ideas of the sensitivity of tumors change as therapeutic methods improve, and certain tumors that formerly were regarded as radio-resistant are today termed radiosensitive.

The radiosensitivity of a tumor depends upon two factors: (1) the histological structure of the tumor, (2) the histological characteristics of the blood vessels and connective tissue which support them. Thus, the radiosensitivity of any neoplasm depends upon its location quite as much as upon the biological structure of its cells.

It was formerly believed that by cutting off the blood supply of a tumor it could be more readily eradicated—in other words, that it could be starved to death. If the surrounding blood supply were destroyed by radiation, it was thought, the tumor would become more radiosensitive. Clinical and experimental evidence have disproved this view. It has been demonstrated that when a tumor's nutrition has been injured by radiation, but complete regression of the growth has not taken place, subsequent attempts to re-radiate the tumor will show it to have become much more radioresistant than it originally was. For this reason it is important that all malignant cells be completely sterilized during the first course of radiotherapy. Even those tumors whose histological structure is very radiosensitive, if inadequately radiated will become increasingly resistant as their cells advance toward maturity and the extent of the growth increases. This increased radioresistance appears

to be due to alterations not only in the malignant cells but in the vascular and connective tissue framework.

Methods of Applying Radiation. There are two general methods by which radiation may be applied: (1) from an external source, the radioactive agent being outside the body so that the radiant energy must pass through the skin or the body tissues; (2) from an internal source, the radioactive focus being introduced directly into the neoplasm.

External irradiation permits the utilization of large portals of entry and makes possible the irradiating of neoplasms so located as to be inaccessible to internal irradiation. Its chief drawback is that it requires the application of high skin doses in order to effect sterilization of the deep-lying tumor cells, and there is always danger that normal neighboring organs or tissues may be injured by the passage of the rays through them.

For external irradiation there must be employed either (1) x-ray or (2) telecurietherapy with radium. X-ray is superior when large radio-sensitive lesions are to be treated but high penetrative power is not essential. Telecurietherapy is best in moderate-sized lesions known to be so radioresistant that high penetrative power must be utilized. As the gamma rays of radium are more homogeneous, selective, and possessed of higher penetrative power, telecurietherapy is the logical choice for radioresistant growths of fairly wide extent, or those subject to regional invasion.

Irradiation of an internal tumor by external radiation requires most careful selection of *portals of entry* for the radiant energy and exact centering of the irradiation on the lesion. The extent of the surface to be irradiated depends, in general, on the size of the growth and the tendency of the tumor to regional invasion. Other factors that require careful consideration, and must be adapted to the particular lesion, are the *filtration* of the irradiating beam, the *distance* between the irradiation source and the lesion, and the *voltage* employed. These depend upon the location and depth of the tumor and the total amount of radiation to be given.

Regarding the *total duration of treatment*, there is no standard practice. Some therapists apply *all* the estimated requirement of energy within 1 or 2 days; others distribute smaller doses over a longer period—for example, Coutard's method, by which small applications of x-ray are made at short intervals over a considerable period.

Considerable success has attended the use of the Coutard method; but

against it may be argued the danger of never administering a single *effective* dose because the individual doses are all too small to bring about sterilization of the malignant cells. On the other hand, if too great a dose is applied at one time, or over a very brief period, the too intense reaction produced in the vascular and connective tissue may make further treatment of the tumor impossible. The *manner of distribution of the total dosage* is, in general, of greater importance than the actual *amount of the total dosage*. Increasing the total dose beyond certain limits reduces rather than increases the chance of sterilizing the tumor. The total dosage and its manner of distribution should always be adapted to the individual patient, and the course guided by careful clinical observation of the effects of radiation upon the tumor, the adjacent tissues and organs, and the general condition of the patient.

Surface irradiation by means of radium at a short distance is applicable to certain malignant lesions, such as cancer of the oral cavity or, in urology, epithelioma of the penis. It is accomplished by the use of radium containers, or molds, made of Columbia paste, dental compound, or vulcanite, shaped for each individual lesion. It permits a homogeneous irradiation that is impossible by other methods and permits irradiation over a long interval. Surface and interstitial irradiation are often combined.

Interstitial irradiation is the method of choice for tumors of limited extent that are accessible to implantation, especially if the tumor is too radioresistant to be sterilized by external irradiation. It is also useful for delivering an intense local irradiation to the base of an accessible lesion that has received previous inadequate external irradiation. Interstitial irradiation has certain definite advantages because it permits the delivery of an intense dose to a small area and because it produces no general reactions or injurious radiation effects upon extensive areas of normal tissues.

Interstitial irradiation is effected by embedding radon needles in the lesion or implanting the tumor with radon seeds.

Radon seeds are made up from fine capillary tubing of glass or gold, which is sealed off into very short lengths (over a Bunsen burner in the case of glass, or by pinching off with pliers if the tube is of gold). The gold seeds, sealed by clamping of the soft metal ends, sometimes leak at the joints, making dosage unreliable and running the risk of burning the tissues by the liberation of unscreened radon. The pinched end is

not smooth, and the seed, if left permanently in the tissue, is likely to prove a source of considerable irritation—obviously most undesirable in a cancerous area. Glass seeds, which cannot leak, are therefore to be preferred. Originally, unfiltered glass seeds were utilized, resulting in an intense caustic and necrotic effect upon both the normal and neoplastic tissues. The introduction of the removable platinum-filtered glass seed by Joseph Muir, shortly followed by the gold-filtered radon seed devised by Failla and Quick, of the Memorial Hospital (New York), greatly facilitated radon implantation. The filtration provided by the metal cuts off the caustic radiation and eliminates, or greatly diminishes, sloughing. The threads attached to the removable seeds serve to indicate where the seeds have been placed, and, after implantation, may be cut off so short as to cause no inconvenience or danger of dislodgment. As soon as the desired amount of radiation has been delivered, the seeds can be withdrawn, so that no foreign body remains in the tissues.

The platinum or gold-filtered seeds are thrust into the tissue by means of a special implanter. The glass radon seeds may also be placed in a platinum needle and this inserted in the tumor.

Irradiation of the Genito-urinary Tract. Because the opinions of different urologists and radiotherapists, on the basis of their experience, still differ widely, it is impossible to give a comprehensive picture of the best practice at present obtaining in the treatment of malignant lesions of the genito-urinary organs. Each of the three available methods—surgery, irradiation, and a combination of surgery and irradiation—has its own particular value. Both x-ray and radium irradiation are widely used in the treatment of tumors of the urogenital tract. At present radon implantation is used extensively in the bladder for the treatment of both papilloma and malignant tumors. It is likewise employed for carcinoma of the prostate, usually after prostatectomy or transurethral resection, though sometimes without previous surgery. Roentgenotherapy is being used increasingly for teratoma of the testis. For epithelioma of the penis and the less common lesions, such as cancer of the male and female urethras, radium and x-ray are both used, but much less often.

In considering a combination of surgery and irradiation, it should be borne in mind that the purpose of *preoperative irradiation* is not the sterilization of the entire tumor, but, rather, (1) to reduce the dissemination of malignant cells during operation by devitalizing the most radio-

sensitive cells preoperatively; (2) to secure information regarding the biological character of the tumor—marked regression during preoperative irradiation indicating that the lesion is radiosensitive. At times, moderate external irradiation of an apparently inoperable growth may cause sufficient regression to render the tumor operable. Preoperative irradiation is at present less widely used in urology than is postoperative irradiation.

Postoperative irradiation is given either as an additional safeguard in cases in which the malignant growth has been apparently removed in its entirety, or as supplementary treatment in patients in whom operation was presumably inadequate.

CARCINOMA OF THE PENIS

In general, radiation has proved of little value in the management of malignant tumors of the penis. Most urologists at present prefer to treat all but very small, superficial epitheliomas by excision of both the primary lesion on the penis and palpable inguinal lymph nodes. The argument for radium, in the treatment of the primary malignant lesion, has been that it is just as effective and much less mutilating than amputation. The first premise is now being questioned. Most tumors of the penis are relatively radioresistant squamous-cell carcinomas. Basal-cell carcinoma of the penis is very rare. For the control of all but the smallest tumors heavy dosage of radon is essential. This is productive not only of great pain, which does not subside for several weeks even in the most favorable cases, but also of extensive fibrosis, which often contracts the penis to such a degree as to render it functionless. This, from the patient's point of view at least, nullifies the chief reason for preferring radium treatment to surgery.

Small growths that have not infiltrated the corpora nor metastasized, are sometimes treated by moderately penetrating and prolonged roentgen therapy or by the surface application of radium, utilizing a radium mold. Almost all therapists agree that when the cavernous structures are deeply infiltrated, surgical treatment, which usually consists of amputation, offers the better prognosis.

Dean, at the Memorial Hospital (New York), believes that superficial tumors no larger than 2 cm. in diameter can be regularly cured by the application of a radium plaque at a distance of 1 cm.; but, if the growth has invaded the cavernous tissues, surgery is preferable. Amputation

1.5 cm. proximal to any visible or palpable involvement has been found sufficient to control the primary growth. Irradiation of metastasis to the inguinal nodes has not been successful. Therefore, when carcinomatous involvement of the nodes has been proved by biopsy, radical excision is done.

Foulds and Stevens, of Toronto, destroy a small lesion of a low grade of malignancy by fulguration and implant radon seeds in the tumor's base, or they sometimes apply a radon pack. Larger growths are amputated, with or without dissection of the inguinal nodes. Sometimes the nodes are merely treated with roentgen radiation. Following total amputation, one or more fairly extensive postoperative courses of deep x-ray therapy to the gland-bearing area are regularly given. Although epidermoid carcinomas are usually not radiosensitive, they consider this procedure "a proper and useful one."

Graves, of Boston, employs surgical excision for removal of the primary tumor, followed by high voltage x-ray therapy directed to the femoral, inguinal, and deep pelvic regions in all cases, whether or not the nodes have been surgically dissected. He does not recommend radiation for the primary malignant lesion.

In 1931 L. G. Lewis reported a series of 34 cases of carcinoma of the penis treated by radical operation; of these, 15 patients were living from 18 months to 16 years after treatment, 8 had died, and 11 could not be traced. Of 62 patients treated by surgery alone at the Mayo Clinic between 1907 and 1932, 7 were well at the time of the report in 1934, of 65 patients treated by a combination of surgery and irradiation, 17 were living; of 19 patients treated by irradiation alone, 3 were alive (Bowing, *et al.*). Of 12 patients with superficial epithelial lesions without metastases, treated at the Memorial Hospital by radium alone, 6 were living 5 to 13 years (Dean, 1935). In a series of 37 cases reported on by Horn and Nesbit in 1934, 11 patients were treated by total amputation of the penis with transplantation of the urethra into the perineum and irradiation of the inguinal nodes; of these, 6 were living from 4 to 8 years after treatment.

We do not advocate the use of radiation alone in any form of penile cancer, whether large or small—preferring partial or complete amputation in the more extensive lesions, with dissection of palpable inguinal nodes (Carcinoma of the Penis, p. 303; Surgical Treatment of Penile

Carcinoma, p. 323). Unfortunately, many of the patients do present these more extensive lesions when first seen. Small, papillary lesions with little infiltration and without metastases may be destroyed by fulguration and radon seeds implanted in the tumor's base.

EPITHELIOMA OF THE SCROTUM

Epithelioma is practically the only form of malignant tumor seen on the scrotum (Epithelioma of the Scrotum, p. 420). Metastasis to the inguinal nodes is likely to occur early in the course of the tumor.

In almost every case surgical removal is the treatment of choice, and can be carried out with safety and success in the majority. The scrotal growth should be excised with a wide margin of healthy tissue and the glands in both groins fully extirpated. The scrotal growth and the tissues of the groin may be removed *en masse* or through separate incisions.

Because of the success of surgery in these cases, radiation is seldom utilized. Moreover, when employing radiation there is always danger of sterilizing the patient, as it is practically impossible to protect the testicle directly beneath the scrotal area to be irradiated. As epithelioma of the scrotum not infrequently occurs in young men, this is an important consideration.

TUMORS OF THE TESTICLE

Most tumors of the testicle are teratomatous in type and are, therefore, highly malignant (Tumors of the Testicle, p. 451). As a rule, they metastasize early through lymphatics and veins, and metastases are present in a high percentage of cases when the patients present themselves for treatment. Metastases grow rapidly and spread widely.

Four principal methods of treatment are available: (1) simple orchidectomy, (2) orchidectomy and irradiation, (3) radical operation, including removal of the regional and retroperitoneal lymph nodes, and irradiation, (4) irradiation alone. Simple orchidectomy is an entirely inadequate therapeutic procedure in most cases. It is never curative when glandular or general metastases have occurred, and is indicated mainly for diagnosis. Wasterlain (1932) found that fewer than 6 per cent of the patients were alive 4 years after simple orchidectomy, and Hinman (1933) found only 17 five-year cures in 258 cases so treated.

The results of surgery by the radical operation have been considerably

better. In a series of 80 cases operated upon by American surgeons and collected by Hinman, 17 (21.2 per cent) were alive and symptomless after 5 years. However, because of the high malignancy and tendency to early metastasis of most testicular neoplasms, surgery alone has never proved very efficient in controlling them.

During the past two decades a number of favorable reports on the use of radiation have appeared. As teratoid tumors of the testicle are relatively rare, it has taken some time to collect enough data to allow the average clinician to form an opinion of the remote results. Comparatively few therapists use radiation before removing the primary tumor, and fewer still use radiation alone; but in most clinics deep x-ray therapy is employed after extirpation of the testicle.

There may be great differences in the structure of testicular teratomas, with corresponding variation in their radiosensitivity. Those who utilize preoperative radiation do so chiefly for the purpose of gaining information regarding the radiosensitivity of a particular growth. Although the radiosensitivity of a tumor can be predicted to some degree by the quantitative determination of the hormone output in the urine, it can be definitely shown, they believe, only by a test of irradiation itself; therefore, the treatment of every testicular tumor should begin with irradiation. In those cases which do not respond satisfactorily, operation following irradiation is indicated, followed by an intensive postoperative course of irradiation of the lymphatic area. In those cases which respond satisfactorily to the irradiation test, further irradiation is indicated; but whether surgery offers additional safety in such cases is still unanswered (Cutler and Buschke).

At the Middlesex Hospital, London, the practice consists in the combination of orchidectomy and prophylactic irradiation (Gordon-Taylor, 1938). "Nowadays," this author states, "the pendulum has swung back from the extended operation to minor surgery and appropriate radiation, and the end-results justify the modern policy." Orchidectomy and radiation, he claims, has proved very effective with seminomas, but has not brought about any noticeable improvement in the high mortality of teratomas. Even with seminomas the results are highly variable, because all growths are not equally radiosensitive. "Where massive metastatic deposits occur, a time comes when radiation becomes impracticable, and recurrences no longer respond to this form of therapy."

At the Memorial Hospital (New York) irradiation is regarded as the best treatment for testicular tumors in all stages of the disease. The

practice there, as reported by Dean in 1939, is as follows: As soon as a teratoma has been diagnosed, irradiation is given to the primary tumor and the lymphatic pathway through which the disease usually spreads. Three exposures of 500 r each, on alternate days, are usually sufficient to effect destruction of the primary tumor and thorough irradiation of the cord. The epigastrium, pelvis, and abdomen on the same side as the diseased testis are also irradiated routinely, whether or not metastases can be found. Two anterior and two posterior portals usually cover these areas, and fractionated doses are given until each portal has received 2,500 r. After irradiation, the primary tumor is measured every 2 or 3 days. When the affected testicle has shrunk to approximately the size of its normal mate (which usually requires 4 to 6 weeks), orchidectomy is carefully performed. If the tumor shows no regression, the testicle is removed earlier. Orchidectomy is performed after irradiation only for the purpose of saving the spermatogenic function of the healthy testis, since complete devitalization of the primary tumor by irradiation usually requires repeated cycles, and this, in spite of careful shielding, is likely to result in permanent loss of spermatogenesis. Metastases, when found, are treated by maximal doses of roentgen rays through numerous portals. The 200 kv. roentgen-ray unit is employed, with 30 ma. of current and filtration of 0.5 mm. of copper and 1 mm. of aluminum. Primary tumors are treated at 50 cm. distance; metastases at 70 cm. In a series of 170 patients with teratomas, 72 per cent of which had metastasized, the five-year end-results after irradiation showed 29 per cent living and free from disease. "On the basis of these results," Dean states, "it seems reasonable to conclude that irradiation is the best treatment for testicular teratomas in all stages of the disease."

Hinman and Powell, in a recent publication (1938), express disapproval of preoperative irradiation because massive doses of x-rays to the primary tumor in the testicle before surgical removal largely destroy the information which can be obtained by the hormonal test and make it impossible to get good histological sections for microscopic study after orchidectomy. "Some cures by irradiation have been reported without orchidectomy—but also without histologic confirmation of the diagnosis." They advocate massive doses of x-ray following orchidectomy, using every care to avoid injury to the remaining testicle. If metastasis appears, or the hormone reappears in the urine, further irradiation of the same order is indicated, even though the consensus of opinion is that no treatment is likely to be of much avail under these circumstances. As metastases

usually appear in the primary and secondary lymph zones of the testicle, these areas should be intensively irradiated, provided that the secondary deposits have been histologically demonstrated to be radiosensitive.

We feel that the radical operation followed by a thorough course of deep x-ray therapy offers the patient the best chance of cure when there are no demonstrable metastases and his general condition is good (*Radical Operation for Tumor of the Testicle*, p. 498). In other cases, orchidectomy followed by deep x-ray therapy directed to the primary and glandular zones is indicated.

MALIGNANT TUMORS OF THE SEMINAL VESICLE AND SPERMATIC CORD

Although the testicle and epididymis are not infrequently involved in a malignant process, the generative adnexa, with the exception of the prostate gland, very seldom develop any form of cancer. Because of this rarity, very little has been published concerning the employment of radiation in these areas.

Most neoplasms of the spermatic cord are benign, and can usually be enucleated without great difficulty or likelihood of recurrence. The majority of recorded malignant growths of the cord are sarcomatous in nature, and sarcoma seldom regresses satisfactorily under radiation.

Fewer than 20 cases of primary carcinoma of the seminal vesicles have been reported, only a handful of which were definitely proved (*Tumors of the Seminal Vesicle*, p. 550). The seminal vesicles are quite frequently invaded by extension from a malignant growth in the prostate, however, in which event they partake in the treatment directed to the primary tumor.

Our experience leads us to believe that all tumors of the seminal vesicle and spermatic cord should be excised whenever possible. Excision should be followed by postoperative irradiation with deep roentgen therapy, or, if the tumor bed is so situated as to lend itself to radon implantation, this form of irradiation may be employed. Such measures would seem to be in order even with sarcomatous tumors, for radiation offers palliation, even when a fatal outcome is inevitable.

MALIGNANT TUMORS OF THE FEMALE EXTERNAL GENITALIA

Neoplasms of the female external genitalia occur sufficiently often to be of considerable clinical importance (*Malignant Tumors of the Vulva*, p. 590); *Malignant Tumors of the Vagina*, p. 599). They are highly malignant, extend rapidly, and early involve the inguinal nodes—usually

on both sides. Recurrence after removal is common. Most authors consider malignant lesions of the vulva and urethra together, because in advanced cases it is often difficult to tell where the tumor originated. Similarly, vulvar and vaginal growths are not always readily separated in so far as the site of origin is concerned.

Epitheliomas make up the bulk of these growths, whether found in the genital or urinary tract. The tumor may originate on the labium majorum or interlabial fold, the labium minorum, clitoris, in a bartholinian gland or duct, or any other portion of the vulva, in the urethra, or in the vagina, particularly the posterior fornix. Extension to the adjacent lymphatics takes place early.

Most vulvar and vaginal tumors are squamous-cell carcinomas. Adenocarcinoma occasionally occurs in the bartholinian glands and other glandular structures about the external genitalia. Sarcomas are very rare. A few cases of primary chorionepithelioma of the vagina have been reported, but usually such growths are secondary to chorionepithelioma of the uterus.

In general, epidermoid growths (such as the squamous-cell variety) are not very radiosensitive. In practice, most therapists have found the treatment of vulvar tumors by radiation to be unsatisfactory, and have had their best results by radical surgery. The delicacy of the normal tissues of the vulva and their extreme sensitivity to radiation make it exceedingly difficult to irradiate the growth satisfactorily without producing serious necrosis of the normal tissues. Vulvectomy with complete bilateral inguinal dissection for the associated adenopathy is therefore the treatment of all operable carcinomas of the vulva.

Taussig, reporting the results in 49 cases of vulvar cancer treated in the *Barnard Free Skin and Cancer Hospital, St. Louis (1929)*, stated that radical surgery had given the most satisfactory results. Cutler and Buschke (1938) also expressed the belief that, in general, radical surgery is the most effective method of treating vulvar cancer, and that irradiation has its place only in inoperable cases or when the lesion is proved to be highly radiosensitive. In small groups of cases they have succeeded in curing very small tumors by means of radium; but they emphasize that the procedure is hazardous and that there is a very narrow limit of safety between the minimum effective dose and the dose which results in radionecrosis.

Some surgeons, who used radium alone in their earlier work, have now substituted electrocautery excision followed by implantation of radon

in the base of the tumor, with x-raying of the entire region as a final precaution. A favorable report on this was made by the Swedish radium therapist, Heyman, in 1932.

The most extensive recent series of irradiated cases of malignancy of the female external genitalia that has come to our attention is that of the Dutch gynecologist, D. den Hoed (1936). This therapist is of the opinion that the same measures are not applicable to both cancer of the urethra and malignancy of the vulva. Surgery is hazardous in the urethra, he believes, because total incontinence may so easily be induced by injury to the sphincter. The labia, however, may be removed with impunity, for they play no part in function. At the Netherlands Cancer Institute radium has not been found suited for use in the vulvar tissues. Tumors of the vulva are removed with the knife or diathermic needle, and roentgen radiation is used both before and after vulvectomy, although not, usually, in any one patient. Radium is occasionally used for postoperative treatment. On the other hand, in the treatment of urethral cancer the tendency is to depend upon radium alone for small tumors, and roentgen irradiation for extensive growths. As a rule, in most cancers of the female external genitals radiation alone has proved the best way to manage the metastatic lymph nodes. Of 57 women treated for vulvar cancer, 20 (35 per cent) lived longer than 5 years.

Radiation of epithelioma of the vulva has been extensively practiced by Jean Cahen, of Brussels, who reported on his work in 1933. In his opinion, cancer of the vulva is not well suited for surgical excision. He thus differs radically from den Hoed and most others. The use of radium needles and of molds fitted to the shape of the affected part, in which tubes of radium or radon were embedded, was the usual first step. In the earlier work at this clinic vulvectomy was later performed; but when examination of the extirpated tissue regularly showed sterilization of all the malignant cells, they eventually abandoned surgical excision and depended solely upon radiation—regional gland metastasis being treated by x-ray or, sometimes, by the application of radium plaques.

The consensus of opinion regarding the best method of treating vulvar cancer appears, therefore, to be as follows: Vulvectomy and bilateral inguinal dissection is to be preferred whenever this is possible. Whether or not irradiation improves the surgical results is unanswered. If surgical excision of the vulvar growth is impossible, removal of the external portion of the tumor with the diathermic needle, followed by the implantation of radon seeds at the base of the tumor and general x-raying

of the entire region is the next best course. For inoperable tumors and recurrences, radium and roentgen rays alone are used.

When the growth is located in the vagina, the same general situation is encountered. Malignant lesions high up in the vagina carry with them the added hazard of vesicovaginal fistula, should extension take place toward the vesical wall. The prognosis is poor in most cases, so that the use of radium or roentgen rays is likely to be chiefly palliative.

D. den Hoed reported on 31 patients with carcinoma of the vagina seen between 1915 and 1932, only 22 of whom had lesions that were "primary, treatable." Of these, 7 (30 per cent) recovered and lived from 20 to 3 years after the treatment, which consisted of radium radiation, with additional x-ray radiation in some cases and, in others, electrocoagulation used as an adjuvant.

MALIGNANT TUMORS OF THE MALE URETHRA

Malignant growths of the male urethra are rare. This is fortunate, as the results of treatment, by any method, have been very unsatisfactory, particularly when the tumor has been located in the less accessible bulbous or membranous portion of the urethra (Malignant Tumors of the Male Urethra, p. 650). The diagnosis in these cases usually has been made only after the growth has become well advanced. Tumors in the cavernous urethra and fossa navicularis are likely to be discovered at an earlier stage and to be more amenable to treatment. In almost all the cases in which an apparent cure has been effected the growth was located in the distal portion of the urethra.

Reports on the use of radium in these cases are very few. Herbst (1925) reported disappearance of a tumor following the use of radium after fulguration had failed. Bierberbach and Peters, on the other hand, found that the use of radium favored necrosis in the growth so that their patient's end was hastened by toxic poisoning. In 1929 Watson, of the Buffalo Cancer Institute, reported on the use of radium in 2 cases. In one, that of a man of 35 years, a five-year cure was effected following a lengthy course of radium applications and intensive x-ray treatment. In the other, under radium applications and x-raying of the urethral area at irregular intervals the 71-year-old patient was enabled to remain in fairly good health for 5 years, and died at the age of 76 years from a cardiac collapse in no way directly connected with the urethral growth, although this was still in evidence at the time of his death. From this limited experience, taking into consideration the subsequent improve-

ment in both radium and x-ray methods, it is reasonable to conclude that radiation will control carcinoma of the male urethra and may even result in permanent regression of some tumors seen early.

In advanced growths, partial or radical amputation of the penis, with extirpation of the inguinal lymph nodes and thorough x-ray irradiation of the inguinal regions and tumor site, appears to offer the best chance of satisfactory immediate results. In late cases, however, any treatment—whether by surgery or radiation—is likely to be merely palliative. In cases seen earlier successful results have been reported from partial amputation of the penis (Boggon; Kretschmer), or resection of the malignant portion of the urethra (Braasch and Scholl; Lower).

A useful method of treatment, in cases seen fairly early, is the application of radium element to the tumor through a rubber catheter until examination shows that the lesion has disappeared. The patient should return for check-up, and if there is recurrence, the application of radium element should again be instituted.

Though preferring radical surgery in advanced cases, we feel that tumors confined to the anterior portion of the penile urethra, and appearing at the urethral meatus, can be treated by more conservative measures than amputation of the entire penile shaft. Electrocoagulation of the tumor mass, supplemented by the implantation of radon seeds in the base, has given satisfaction in a few instances where the lesion came early under treatment. Recurrences should be controlled by radium and roentgen therapy.

MALIGNANT TUMORS OF COWPER'S GLANDS

Because malignancy of Cowper's glands is apparently extremely rare (only 6 authenticated cases having been published), there is almost nothing in medical literature concerning the radiation treatment of this lesion. It would seem to us, however, that the best method of dealing with a tumor of these glands would be by as complete excision as possible by the perineal route, followed by the implantation of radon seeds and deep roentgen therapy (Carcinoma of Cowper's Glands, p. 742).

In the fifth authenticated case to be recorded (Uhle and Archer, 1935) excision of the neoplasm through the perineum was followed by the insertion of radium needles throughout a small portion of the tumor mass which could not be removed. These were removed on the seventh day after having delivered a total dosage of 806.4 mgm. hours of gamma radiation. A course of deep x-ray therapy was subsequently given—a

total of 1331 roentgen units being administered through each of 3 portals (right and left inguinal regions and the lumbosacral region) and a total of 800 roentgen units through each of 2 portals (lower thoracic and the entire lumbar spine). Apparently complete clinical regression was obtained, for one year after operation the patient was still well and had gained weight.

In the most recently reported case (Gutierrez, 1937) it is recommended that as soon as histological examination of the specimen removed has proved the presence of a malignant growth, the operation should be followed by the implantation of radon seeds in the perineum and deep x-ray treatment. Gutierrez himself did not employ these measures, because his patient died of pulmonary complications 3 weeks after operation.

MALIGNANT TUMORS OF THE FEMALE URETHRA

During the last 15 years, radium has been employed with steadily increasing frequency in combating carcinoma of the female urethra. Some good results have been reported in cases observed early; but the high degree of malignancy of these tumors, the late stage at which many are seen, and the advanced age of the majority of the patients make the prognosis in most cases poor.

In a very complete review of the literature (Sparks and Parsons, 1937) there are listed 119 cases of primary carcinoma of the female urethra, practically all of which were reported after radium had been introduced into medicine. Of the 40 patients treated by irradiation alone, 7 were living 3 years or more after treatment, and 5 were living 5 years or longer. Of the 21 women first operated upon and later treated with radium or deep x-ray, 7 lived more than 3 years and 5 more than 5 years. These results are conspicuously better than anything obtained by surgery used alone.

Because of the rarity of this lesion, reports on large series of cases are not to be had, so that the merits of any particular method of applying radiation cannot be adequately compared. Sparks and Parsons concluded from their study of current case reports that the best procedure is to destroy the primary tumor by radium, x-ray, or excision (in the order named) and remove the involved lymph nodes by surgery. Radon implants have been successfully used at the Memorial Hospital, in New York. The highest percentage of five-year cures were obtained in the Mayo Clinic series when radium and roentgen rays were used.

In 1923 Pomeroy treated a woman suffering from urethral carcinoma with surface applications of screened radium element, with an additional short irradiation by means of steel needles of relatively large radium content. This patient was alive and well 15 years later. Another, treated by surface applications of screened radium, followed 3 months later by limited cautery excision, was alive without recurrence 10 years after treatment.

Den Hoed, of the Netherlands Cancer Institute, favors the use of radiation alone in primary tumors of the female urethra. In this clinic, surface applications of radium are used for small, circumscribed tumors of the female urethra, with occasional employment of needles if the growth has penetrated toward the bladder. Extensive growths are treated by roentgen rays.

Auer (1935), reporting the results in 7 early cases, in 2 of which the patients lived more than 5 years, concludes that local irradiation to the primary lesion, with or without cautery excision, and dissection of the inguinal nodes is the treatment of choice in early and moderately advanced cases. Watson (1936) has also reported good results with electrocoagulation or radium irradiation to the primary tumor, but treats the adenopathy by roentgen irradiation.

The preferred treatment, it seems to us, is as complete excision of the primary tumor as possible followed by implantation of radon seeds in the base. If the inguinal lymph nodes are involved, they should be surgically removed and deep x-ray applied postoperatively. Deep x-ray treatment should be given to the inguinal regions as a precautionary measure even if there is no evidence of their involvement. We prefer the implantation of radon seeds in the base of the tumor to surface applications of radium because this method causes less necrosis and distributes the rays evenly throughout the growth.

Radical removal of the urethra is usually done only as a last resort, since this necessitates transplanting the ureters.

RADIATION TREATMENT OF BENIGN HYPERTROPHY OF THE PROSTATE GLAND

The idea that benign hypertrophy of the prostate might be reduced by suitable radiation early occurred to workers both in urology and radiotherapy, but it is only during the last decade or so that it has received serious consideration. There is a great diversity of opinion as to the effect of such treatment.

Relief of retention by the use of deep roentgen radiation has been reported by Schiller and Altschul (1930); Barringer and his co-workers at the Memorial Hospital (1934), who reported a distinct decrease and control of the edema of the prostate, with reduction or abolishment of the residual urine, in 30 per cent of their cases; and by K. Abel (1936), who gained subjective relief for 26 of the 35 patients he was able to follow up for an extended period. Henningsen (1936) and V. Blum (1936) found roentgen radiation valueless in reducing prostatic hypertrophy. The former, however, had great success with radium applied through the urethra.

Burnam, of Johns Hopkins, in 1938 reported marked relief of retention and other symptoms associated with prostatic hypertrophy in 30 of 68 patients treated with telerradium therapy. In some cases that were failures from the point of view of relief of retention there was definite reduction in the size of the gland. The dosage varied from 10 mgm. hours administered through the perineum to 60 mgm. hours introduced through 3 portals of entry.

In administering roentgen therapy the usual practice is to employ a 200 kv. machine, with filtration of 0.5 mm. of copper and 1 mm. of aluminum, at 50 cm. skin-target distance. The total dosage at each exposure varies from 200 to 300 roentgens. The treatments are given 3 times a week until 1,000 to 1,500 roentgen units have been administered. If necessary, the treatment-cycle is repeated after an interval of about 6 weeks. Some patients respond satisfactorily to little radiation, while others require more.

In general, the effect of radiation is an alleviation of the associated edema and congestion, with relief of retention, reduction or abolishment of the residual urine, and improvement in functional renal tests. This improvement, from a single course of treatment, may be only for a few years.

From a histological study of 12 cases, Moore (1939) found only minimal changes that might be attributed to roentgen irradiation: slight periacinar fibrosis and a relative absence of lymphoid tissue and evidences of inflammation.

The reports of various urologists and radiotherapists indicate that in the dosage at present administered (1,000 to 1,500 roentgens) x-ray therapy, while useful in certain cases of benign hypertrophy as a form of local treatment for the relief of retention and other symptoms, cannot be regarded as a substitute for resection or prostatectomy. However,

the benefits thus far achieved from the use of both roentgen and radium irradiation in selected cases would seem to warrant further experimentation with these agents in the treatment of benign hypertrophy.

CARCINOMA OF THE PROSTATE GLAND

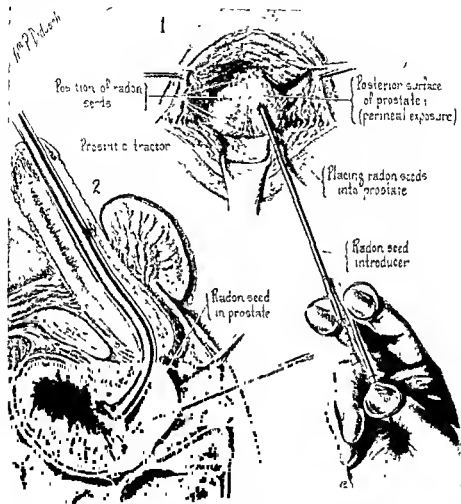
At the present time, the only hope for cure of prostatic carcinoma is early perineal total or subtotal prostatectomy, if the disease has not extended beyond the confines of the prostate and periprostatic tissues (Carcinoma of the Prostate, p. 857). Irradiation, though widely used, must still be considered a palliative measure. The difficulties involved in proper irradiation of the carcinomatous prostate have been and still are very great. The tumor is of a radioresistant glandular type, and the disease is almost always far advanced when discovered.

Prostatic carcinomas differ fairly widely in malignancy. One type, the fibrotic tumor usually found in men over 65 years of age and in prostates that have long been the sites of benign hypertrophy, runs a relatively benign course and is frequently discovered only upon removal of the prostate because of the benign hypertrophy. Patients may survive with these tumors for years without treatment. Metastasis by direct extension occurs comparatively late or not at all. There is a smaller group of highly anaplastic tumors which are usually found in men of about 55 years and in prostates that have undergone little hypertrophic change. These tumors metastasize early and widely to bones and other organs and run a rapid course. Between these two extremes are intermediary types of growths. Very little is known of the response of different cellular types of prostatic carcinoma to irradiation.

Though complete surgical removal is admittedly the best treatment of prostatic carcinoma, unfortunately it can be applied to only a small percentage of the cases. In other cases, in which there is obstruction to the outflow of urine, relief of obstruction by conservative perineal prostatectomy or transurethral resection of the lateral and median lobes, followed by irradiation, probably has most to offer the patient at present.

Although definite cures of prostatic carcinoma by irradiation have not been obtained, its value in prolonging life and alleviating discomfort is recognized by practically all therapists. Deep x-ray therapy is a valuable treatment for the relief of pain caused by metastasis to bones—relief being often obtained by small doses. External radiation therapy, interstitial irradiation applied by the perineal or the suprapubic route, and

local radium application through the open bladder, urethra, or rectum are all used in the treatment of prostatic carcinoma.



in the resected area)

It is possible, by external irradiation, to reduce the size of the prostate and to relieve the obstructive symptoms in some patients whose tumors are beyond radical surgery. It is generally conceded, however, that external radiation by the 200 kv. machine is not enough to control the great majority of prostatic carcinomas. Even Coutard's method.

which is widely regarded as the best at present available, and which gives 300 roentgens daily through 4 or 5 portals until each portal has received 1,500 to 1,800 roentgens, is not sufficient to check cancer of the prostate. Therefore, deep x-ray therapy must be supplemented by interstitial irradiation if substantial regression is to be hoped for. Either radium needles or radon seeds may be used.

Suprapubic implantation of radon seeds into the prostate is a comparatively simple matter if one desires to reach the lateral and subtrigonal lobes; but the posterior lobe, which lies entirely below the bladder, presents a different problem. The posterior lobe is almost always involved in the growth, and suprapubic implantation must be supplemented by perineal treatment if the irradiation is to be adequate.

The original method of inserting radium needles in the prostate through the perineum is still widely used. Although the posterior lobe, periprostatic tissue, and the perilymphatic invasion around the seminal vesicles can be thoroughly irradiated by this method, the "blind" procedure has its limitations, since the needles cannot be accurately placed in the deeper portions of the gland.

The present practice at the Memorial Hospital (Dean, 1939) is to insert two needles of about 50 millicuries each in the uppermost limits of the tumor, one on each side. Six hours later, when 600 millicurie hours have been delivered, each needle is withdrawn the distance of its radon-containing portion and left until another 600 millicurie hours has been given, thus thoroughly irradiating the posterior portion of the tumor. Gold seeds are deposited in the same way. With a needle in the upper limit of the tumor, a seed of about 1.5 millicuries is deposited, then the needle is withdrawn and another seed is deposited, and so on until one seminal vesicle and one side of the prostate are treated at a sitting. About 2 weeks later, the other side is similarly treated. It is better, they feel, to give smaller doses at longer intervals even if several months are required to treat the entire tumor. By this method, there has often been brought about considerable fibrosis in the tumor and diminution in its size without serious reactions.

We feel that, whenever possible, exposing the prostate through a perineal incision and implanting radon seeds through its capsule is preferable, as the entire procedure can then be carried out under full vision. Therefore, in cases with obstruction we either do a conservative perineal prostatectomy and implant radon seeds, or a transurethral resection followed by implantation of seeds through a perineal incision. By

utilizing Kirwin's measuring instrument and radon seed implanter (Figs. 360 to 365) over-radiation can be avoided and the seeds accurately spaced. If open operation is out of the question, endoscopic implantation of the prostate is quite feasible, for the operator's finger in the rectum can guide the needle point of the implanter after it has been plunged through the skin of the perineum under local anesthesia. Even by this "blind" method the seeds can be spaced accurately and over-radiation avoided.

Perineal exposure of the prostate and implantation of removable radium needles is preferred by Young, as well as by Chauvin, in cases that are not amenable to radical surgery.

Marked benefit from the use of high-voltage roentgen irradiation, in the relief of pain and obstructive symptoms, has lately been reported by Smith and Pierson, at the Massachusetts General Hospital, Mudd and Emery, and Widman, of the Philadelphia General Hospital. Widman, reporting the results of irradiation in 82 cases of prostatic carcinoma, expresses the opinion that the recommendation of high-voltage irradiation for advanced carcinoma of the prostate is justified in every case in which the patient's condition is sufficiently good to tolerate intensive treatment. This author believes cancer of the prostate to be essentially a radiologic problem, and that in selected early cases interstitial radiation with gold seeds or platinum needles should offer great possibilities of improving the end-results.

TUMORS OF THE BLADDER

Tumors of the bladder are considered on page 1037. Treatment of vesical neoplasm by any method—surgery, fulguration, or irradiation—is at the present time unsatisfactory, due chiefly to the late diagnosis and the great tendency of these tumors to recur following removal.

Since vesical cancer remains localized within the organ for a considerable time before metastasis occurs, surgical excision would seem to be the ideal method of treatment. However, a majority of bladder tumors are located in the trigone, or lower lateral or posterior walls, where their surgical removal would involve the sacrifice of one or both ureters or the urethra; therefore, excision is often impossible. Elsewhere we have stated that, in our opinion, surgically accessible malignant tumors should be radically excised, and that occasionally, in carefully selected cases, cystectomy with transplantation of the ureters is indicated. When surgical excision is not possible, we remove the exuberant portion of the

tumor by electrocoagulation (transurethrally or through the open bladder) and implant radon seeds in the base with a special implanter designed by Kirwin. In company with most other urologists, we have not found irradiation, used alone, satisfactory.

Application of Radium. Use of Radon Seeds. The most effective irradiation of the bladder thus far has been given by implanted radon seeds. William Duane and R. B. Greenough of Boston, and B. S. Barringer, of New York, were pioneers in the use of radon in the bladder and the bladder neck (1917-1919), and in the two decades that have since elapsed radon has been used more and more in the treatment of vesical malignancy. Removable radium needles and surface applications of radium also have been used, but have not proved as satisfactory as the seeds.

Seeds may be implanted (1) transurethrally, through the cystoscope, or (2) suprapubically, through the open bladder. The papillary portion of the tumor is usually removed with the cautery or by simple fulguration, exposing the base of the tumor for implantation with seeds.

The use of removable platinum or gold-filtered glass radon seeds has greatly facilitated radium implantation in the bladder. The attached threads serve to indicate where the seeds have been placed, and are cut off before the seeds are inserted in the loading slot of the implanter, leaving only 1 cm. to project from the channel of insertion. As soon as the desired dosage has been given, the seeds can be withdrawn with the cystoscopic forceps.

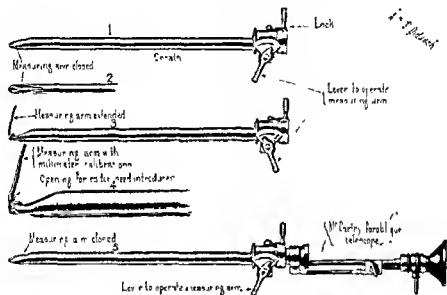
Methods of Implantation. *Implantation through the cystoscope* (closed method) is very satisfactory when the tumor is small (about 2 cm. in diameter), plainly visible, and readily accessible to the cystoscope. It is also preferable in patients whose poor systemic condition prohibits any type of open operation. *The suprapubic approach* is preferable for large, poorly visualized, or multiple growths; for tumors situated near the urethral orifice and inaccessible to the cystoscope; when cystitis or hemorrhage renders cystoscopy difficult or impossible; for infiltrating tumors, even of small size, when the extent of submucous extension cannot be accurately gauged through the cystoscope.

Kirwin Measuring Instrument and Radon Seed Implanter. With the assistance of Mr. F. C. Wappler, Kirwin has designed a *measuring instrument* to determine the dimensions of the tumor to be treated, and also an *implanter*, by means of which radon seeds may be introduced into bladder tumors, by either the endoscopic or open route, in less time and with

greater facility than has heretofore been possible. These instruments, with the modifications making them adaptable to the special conditions of the individual case, are shown in figures 360 to 365.

Combined Use of Radium with Electrocoagulation or Surgery. We do not employ radiation alone in the treatment of bladder tumors, but regularly make use of combination methods.

Until malignant degeneration sets in, fulguration is a specific treatment for papilloma; but when malignant changes occur, electrosurgery alone



is not sufficient and must be supplemented by radiation therapy or the tumor must be radically excised.

The treatment of bladder tumors by surgery and fulguration is described under *Operative Treatment of the Bladder* (pp. 1106 and 1146). These methods, it will be noted, are supplemented by irradiation.

In the "clamp method" used by us for the surgical removal of bladder tumors, radon seeds are inserted in the cut edges of the bladder wall before closure as a precautionary measure (Fig. 243).

In the "loop-ball-disc" (open) method of handling large tumors not accessible to radical resection, the ball electrode is first applied to the

wall encircling the tumor, to seal off the vessels, the entire overgrowth removed with the loop electrode, and the disc electrode applied to the base of the tumor, leaving a smooth surface for the implantation of radon seeds. The seeds are implanted 2 cm. apart into the base and the wall of the bladder around the base with the Kirwin implanter (Fig. 268).

In the transurethral (closed) method, suitable for smaller tumors, the size of the growth is first ascertained by the Kirwin measuring instru-

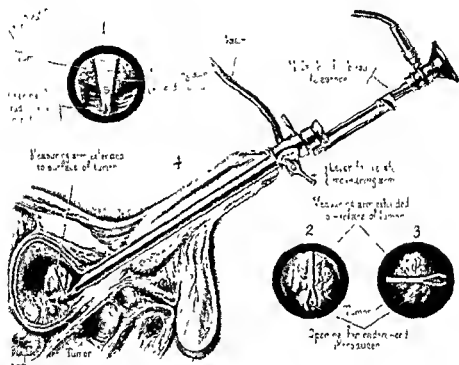


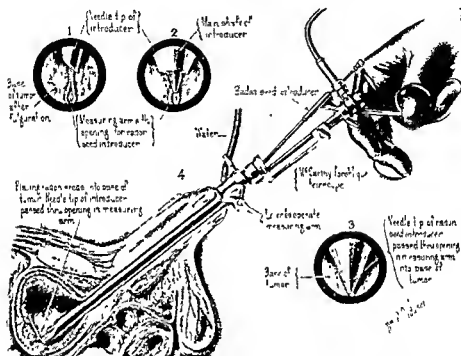
FIG. 268. Kirwin measuring instrument. Postoperative appearance of the measuring arm.

after fulguration of the exuberant portion of the growth. (4) The appearance of the instrument after passage through the urethra.

ment, and the correct amount of radon dosage estimated. The exuberant portion of the tumor is then removed with the Kirwin resectoscope, so that the base may be fully exposed for radon implantation. Application of the disc electrode will leave a clear surface ready to receive as many seeds as the measuring instrument has indicated to be necessary (Fig. 362).

Roentgen Irradiation of Bladder Tumors. External roentgen irradiation

tion is used most often in conjunction with some other therapeutic method in the treatment of bladder tumors, or for palliation only in the treatment of patients with inoperable lesions. Because of the thickness of the tissues intervening between the source of irradiation and the tumor, it has not proved possible to deliver curative doses of deep x-ray to bladder tumors without seriously damaging the bladder, rectum, and



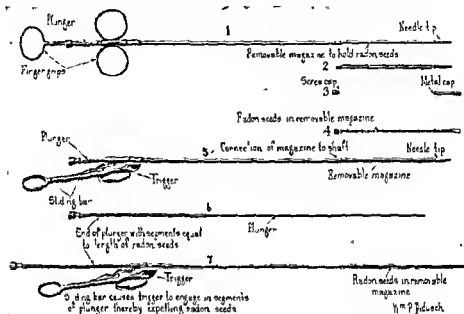
adjacent tissues. Recently, direct irradiation of vesical neoplasms has been tried, but it is too early to mention end-results.

When deep x-ray therapy is used, it is usually in one of the following combinations:

- (1) Excision, followed by deep x-ray therapy.
- (2) Preliminary roentgen therapy, local extirpation, followed by deep roentgen therapy at a later date.
- (3) Preliminary roentgen therapy, followed by radon implants.

- (4) High-voltage roentgen therapy with heavy filtration, with the addition of transurethral electrocauterization in certain cases where it is believed that some part of the tumor has not been rendered harmless by the preceding irradiation.

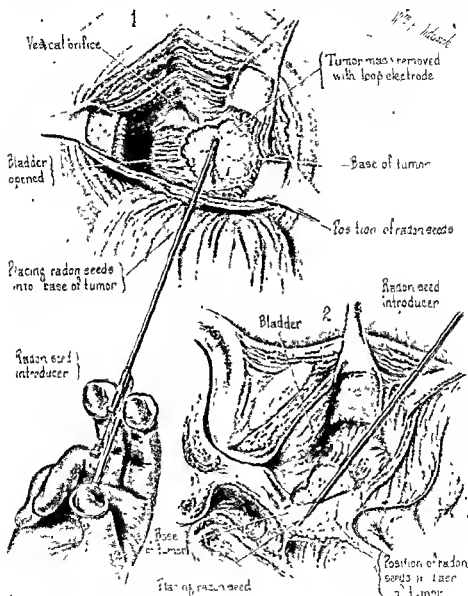
The problem involved is how to deliver enough irradiation into the tumor area to sterilize the cancer cells (3,000 to 6,000 roentgens) without causing serious or permanent injury to the normal tissues.



tent of radon seeds ready for use.

Pfahler has found that by giving treatment through as many portals as possible, which permits accurate cross-firing on the disease, and by delivering 200 to 250 roentgens daily, or 150 roentgens twice daily, less injury to the normal tissues will take place and better results will accrue. He has found pneumocystograms of great help in concentrating the rays directly upon the tumor and the surrounding tissue which may be involved in the malignant process. The treatment is checked from day to day and the indication, as offered by pneumocystography and cystoscopy, carefully followed. In general, hematuria ceases within

though not without merit, should be reserved for such tumors as could not be surgically removed. However, in a personal communication re-



ceived just prior to the publishing of our first edition (more than a year after the presentation before the Genito-Urinary Surgeons) Dr.

Colby stated that bladder tumors treated by external radiation, constant potential, have responded better than have similar growths when treated with lower voltage units. Well-marked regression was noted in about 50 per cent of the cases, pain, frequency, and bleeding being relieved in about the same percentage. He still felt doubtful, however, as to the actual *cureative* value of this supervoltage treatment in vesical tumors. It is still in the experimental stage, and should not yet be regarded as a substitute for surgery, but only as an alternative when surgery is inadvisable or impossible.

Precautions to Be Observed in Irradiating Bladder Tumors. All radiation treatment should be preceded by a careful study of the blood. Previous to undertaking treatment by any means, transfusion is now regularly employed as a precautionary measure in all cases of bladder tumor where hemorrhage has been severe. There is considerable risk in administering large doses of radium to an exsanguinated patient, as even under normal conditions a certain lowering of the hemoglobin content of the blood is inevitable. When x-ray is employed the dosage is fractionated and treatment given over a considerable period. This lessens the danger of inducing a profound anemia.

Deep x-ray treatments must be properly spaced and the dosage graded according to the individual patient's needs and power of resistance. The patient must be kept under strict surveillance and the results of treatment checked from day to day.

TUMORS OF THE KIDNEY AND URETER

Tumors of the kidney may be divided as follows:

- (1) Tumors of the renal pelvis
- (2) Tumors of the renal parenchyma
 - (a) Embryonal or teratoid tumors in children (Wilms' tumor)
 - (b) Tumors occurring in adults (usually after the fortieth year)

Irradiation of Tumors of the Renal Pelvis and Ureter. Tumors of the renal pelvis are much less common than those of the parenchyma. Pelvic and ureteral tumors are chiefly papillomas, papillary carcinomas, and epidermoid carcinomas microscopically similar to those of the bladder, and are radioresistant. Since they spread early and metastasize to the regional lymph nodes and distant organs, and since they usually cause urinary obstruction and infection, prompt nephrectomy, with removal of the ureter and that section of the vesical wall containing the intramural portion of the ureter, is at present the only treatment offering

a hopeful prognosis. The relatively rare squamous-cell carcinomas of the renal pelvis show little tendency to spread to the ureter and bladder, so that removal of the adjacent portion of the ureter with the kidney usually suffices. No five-year cure has been reported in a case of this type. The primary mortality of all pelvic and ureteral tumors is high, and the late mortality is even higher, since recurrence is very common. (Tumors of the Renal Pelvis: Treatment, p. 1552.)

We know of no reports concerning irradiation of tumors of the renal pelvis or ureter.

Irradiation of Wilms' Tumors. The Wilms' tumor is a mixed growth of embryonal origin. It is very malignant, grows rapidly, and metastasizes fairly early. The tendency to recurrence is very marked. Most renal tumors occurring in the first decade of life are of this type, but in adults the Wilms' tumor is rarely encountered. The prognosis in most cases is very poor because of the highly malignant nature of the tumors and the fact that the lesion is usually well advanced by the time the diagnosis is made. The only hope of cure lies in early diagnosis. Thus far, the results of surgery alone have, with rare exceptions, been poor (Wilms' Tumor: Prognosis and Treatment, p. 1559).

In recent years, the treatment of Wilms' tumor by deep roentgenotherapy has received considerable study. Since such growths vary greatly in their structure, there is probably a corresponding variation in their radiosensitivity. Pronounced regression has followed irradiation in many cases, but local recurrence or metastasis is the almost invariable rule. No comprehensive studies of the end-results are as yet available; but experience with this relatively new method of treatment to date indicates that roentgenotherapy alone is not curative, but is a useful palliative measure in inoperable cases and in postoperative recurrences and metastases. Some tumors, considered inoperable, have been reduced sufficiently by irradiation to be rendered operable; but while the immediate operative mortality has been lowered by irradiation, the end-results have not been improved. Cutler and Buschke, in 1938, reported a case in which the child was alive and well 7 years after telecurietherapy of an extensive inoperable Wilms' tumor with metastases of the axillary lymph nodes, and Dean (1939) stated that he knew of 3 patients apparently free of disease between 3 and 5 years after irradiation. Thus far, these happier results have been exceedingly rare.

Because surgery alone has practically no benefits to offer these patients at the advanced stage in which the majority of Wilms' tumors are

discovered, and because—clinically at least—most of these tumors are radiosensitive, Deao has recently recommended that a serious attempt be made to treat all such tumors with external irradiation therapy alone. Formerly he was of the opinion that all Wilms' tumors confined to the kidney should be irradiated and then removed, whereas if metastasis had occurred, irradiation alone should be used; but his experience has shown that "even after sufficient irradiation has been given to cause disappearance of the tumor and an apparently complete nephrectomy has been performed, local recurrences or metastases usually follow."

When roentgen irradiation of Wilms' tumors was first utilized, a single massive dose, or several large doses in a short period of time, was the method employed. The later trend has been toward the fractional method, whereby smaller doses are given over a longer period. Barringer is of the opinion that in Wilms' tumors the regression following irradiation may be permanent if the roentgen therapy is given in a series of very small doses and continued over a long period of time.

In many clinics, preoperative irradiation, nephrectomy, and post-operative roentgenotherapy is now the preferred plan of treatment. Sufficient time has not elapsed, however, for the determination of the superiority of this therapeutic plan over the older method of immediate nephrectomy, with or without postoperative irradiation.

Irradiation of Parenchymal Tumors in Adults. The common parenchymal tumor in adults is carcinoma. Sarcoma is infrequent and Wilms' embryoma very rare. Three varieties of carcinoma are seen: (1) adenocarcinoma, (2) alveolar carcinoma, and (3) malignant papillary cystadenoma. Because their clinical behavior is fairly uniform, it is customary to consider all types of parenchymal carcinoma as a clinical entity (*Tumors of the Renal Parenchyma in Adults* p. 1562).

Renal carcinoma is supposedly radioresistant. Actually, very few pathological studies have been made of tumors removed after irradiation, so that little is definitely known regarding the changes produced by irradiation in these growths.

That malignant tumors of the kidney are not curable by deep x-ray therapy alone is the opinion of practically all urologists and radiotherapists at the present time. Most urologists feel that radiation alone should be reserved for cases of unquestionably inoperable tumor. Nephrectomy offers the only hope of cure in renal neoplasia, and should be done whenever (1) the tumor is confined to the kidney and there

are no definite signs of metastasis, (2) the general condition permits, and (3) there is no marked insufficiency of the other kidney.

Regarding the value of preoperative and postoperative irradiation, there is a division of opinion. Some authors feel that preoperative irradiation has little value and merely delays surgery, sometimes permitting metastases to occur. Others who have tried it claim that it induces fibrotic changes in cortical tumors and facilitates their removal (Walters, Lewis, LeComte, Wharton, and others); that it helps to prevent the dissemination of tumor cells during nephrectomy, and retards metastases.

Postoperative irradiation has found more general favor than preoperative irradiation, and seems to be indicated in cases presenting extrarenal involvement and in those cases in which it has been impossible to remove the entire growth. However, if the tumor has been only partially removed, deep roentgen therapy may retard but will not prevent recurrence.

We feel that whenever the tumor is presumably operable nephrectomy should be done at once, without irradiation. In large lesions, it is frequently very difficult or impossible to determine the operability of a tumor from the clinical and roentgenological findings. It is in these cases, many urologists and radiotherapists feel, that preoperative irradiation is justified in an attempt to reduce the size of the tumor and diminish the operative risk. As soon as sufficient regression has taken place to make the tumor presumably operable, nephrectomy should be done, as such regression is only temporary.

BIBLIOGRAPHY

- ABEL, K.: Die roentgentiefenbestrahlung der prostatahypertrophie. *Beitr. z. klin. Chir.*, 164: 396, 1936.
- ANDREWS, J. R., AND UHLE, C. A. W.: Evaluation of surgery and irradiation in the treatment of vesical cancer. *Am. J. Cancer*, 26: 507, 1936.
- ASPINWALL, A.: Primary epithelioma of the scrotum. *M. J. Australia*, 2: 653, 1931.
- AUER, E. S.: Cancer of the female urethra. *Am. J. Obst. & Gynec.*, 30: 318, 1935.
- BARRINGER, B. S.: Treatment by radium of carcinoma of the prostate and bladder. *J. A. M. A.*, 67: 1442, 1916.
- BARRINGER, B. S.: Radium treatment of carcinoma of the bladder. *Ann. Surg.*, 74: 751, 1921.
- BARRINGER, B. S.: Extension of life in genito-urinary carcinoma: bladder, prostate, penis, testicle. *Kansas City Clin. Soc. Month. Bull.*, 1926.
- BARRINGER, B. S.: Phases of pathology, diagnosis, and treatment of carcinoma of the prostate. *J. Urol.*, 20: 407, 1928.
- BARRINGER, B. S.: Carcinoma of the bladder. *Surg. Gynec. & Obst.*, 58: 867, 1934.
- BARRINGER, B. S.: Radium treatment of cancer of the bladder. *Ann. Surg.*, 101: 1425, 1935.

- BARRINGER, B. S.: Treatment of prostatic carcinoma. *Surg. Gynec. & Obst.*, 52: 410, 1936.
Also: *Am. J. Roent.*, 37: 49, 1937.
- BARRINGER, B. S.: Radiosensitive kidney tumors. *J. Urol.*, 38: 1, 1937.
- BARRINGER, B. S., *et al.*: Roentgen treatment of benign hypertrophy of the prostate gland. *Am. J. Roent.*, 31: 350, 1934.
- BARRINGER, B. S., DEAN, A. L., JR., FERGUSON, R. S., AND KEYES, E. L.: Cancer of the bladder. *J. Urol.*, 31: 423, 1934.
- BELT, ELMER: Carcinoma of the prostate treated by high-voltage x-ray. *Trans. Western Branch Soc. Am. Urol. Assoc.*, 5: 263, 1936.
- BELT, ELMER: Tumors of the testicle. *Am. J. Surg.*, 38: 201, 1937.
- BIERBERBACH, W. D., AND PETERS, N. N.: Primary epidermoid carcinoma of the male posterior urethra. *J. Urol.*, 22: 105, 1929.
- BIRKETT, G. E.: Radium Therapy; Principles and Practice. London, Cassell & Co., Ltd.
- BLOOM, W.: Bericht über maligne Hodengeschwülste. *Strahlentherapie*, 53: 611, 1935.
- BLUM, V.: Fortschritte und wandlungen in der behandlung der prostatahypertrophie. *Med. Klinik*, 32: 111, 1936.
- BOGGER, R. H.: Carcinoma of the male urethra. *Brit. J. Surg.*, 20: 640, 1933.
- BORDIER, H.: Sur le traitement radiothérapique de la hypertrophie de la prostate. *Monde méd.*, 44: 921, 1934.
- BOTHE, A. L.: Effect of roentgen therapy upon tumors of the kidney. *Am. J. Roent.*, 33: 529, 1935.
- BOTHE, A. E.: Roentgen therapy in the treatment of bladder tumors. *J. Urol.*, 36: 643, 1936.
- BOWING, H. H., FRICKE, R. E., AND COUNSELLER, V. S.: Results of treatment of carcinoma of the penis. *Radiol.*, 23: S74, 1934.
- BURNAM, C. F.: The use of radium and roentgen irradiation in benign hypertrophy and cancer of the prostate. *Am. J. Roent.*, 39: 75, January 1938.
- BURNAM, C. F., AND NEILL, WILLIAM, JR.: Treatment of benign hypertrophy of the prostate with radium. *Urol. & Cutan. Rev.*, 28: 261, 1924.
- CAHEN, J.: Le traitement des épithéliomas de la vulve. *Le Cancer*, 10: 62-104, Part II, 1933.
- CAULK, J. R.: Tumors of the renal pelvis and ureter. *Ann. Surg.*, 106: 68, July 1937.
- CHAUVIN, E.: Resultes de la curiethérapie dans le traitement des cancers prostatiques. *Bull. Soc. franc. d'uro.*, p. 212, 1932.
- COLBY, FLETCHER H.: Supervoltage radiation in the treatment of bladder tumors. *Trans. Genito-Urin. Surg.*, p. 225, 1939.
- COLBY, FLETCHER H.: Evaluation of the supervoltage treatment of bladder tumors. (Read at the Annual Meeting of the Am. Urol. Assoc., Buffalo, N. Y., June 21, 1940). *Personal communication.*
- COUNSELLER, V. S., AND PATERSON, S. J.: Carcinoma of the female urethra. *J. Urol.*, 29: 587, 1933.
- COUTARD, H.: Results and methods of treatment of cancer by radiation. *Ann. Surg.*, 106: 584, 1934.
- CUTLER, MAX, AND BUSCHKE, FRANZ: *Cancer: Its Diagnosis and Treatment*. Phila., W. B. Saunders Co., 1938.
- DEAN, A. L., JR.: The treatment of teratoid tumors of the testis with radium and the roentgen ray. *J. Urol.*, 21: 83, 1929.
- DEAN, A. L., JR.: The use of radium and the roentgen rays in the management of cancers of the genito-urinary organs. *New England J. Med.*, 208: 1078, 1932.
- DEAN, A. L., JR.: Radiation treatment of the more common kidney tumors. *Am. J. Roent.*, 38: 80, 1937.

- DUANE, WILLIAM: Methods of preparing and using radioactive substances in the treatment of malignant disease, and of estimating suitable dosages. Boston M. & S. J., 177: 787, 1917.
- DUANE, WILLIAM, AND GREENOUGH, R. B.: *Report of results of radium treatment at the Collis P. Huntington Memorial Hospital by the Cancer Commission of Harvard University.* Boston M. & S. J., 177, 359, 1917.
- FARRELL, J. F., AND FETTER, T. R.: Roentgen irradiation in carcinoma of the bladder. J. Urol., 37: 133, 1937.
- FERGUSON, R. S.: Studies in the diagnosis and treatment of teratoma testis. Am. J. Roent. & Rad. Ther., 31: 356, 1934.
- FERGUSON, R. S.: Infiltrating cancer involving the trigone; treatment. Am. J. Surg., 38: 137, 1937.
- FOULDS, G. S.: Epithelioma of the male urethra. Urol. & Cutan. Rev., 42: 634, 1938.
- FOULDS, G. S., AND STEVENS, B. W.: Cancer of the penis. Brit. J. Urol., 9: 368, 1937.
- FRUCHARD, H.: De l'utilisation des radiations dans les cancers de la vessie et de la prostate. J. d'Urol., 39: 97, 1935.
- GOLDSTEIN, A. E., AND ABESHOUSE, B. S.: Primary carcinoma of the male urethra. Ann. Surg., 105: 213, 1937.
- GONZALES-MARTINEZ, J.: Progress, indications, technic and successful results of radiotherapy in prostatic hypertrophy. Radiol., 24: 66, 1935.
- GORDON-TAYLOR, G., AND TILL, A. S.: On malignant disease of the testicle. Brit. J. Urol., 10: 1-45, March 1938.
- GRAVES, R. C.: Treatment of malignant disease of the penis. J. Urol., 32: 501, 1934.
- GUTIERREZ, R.: Primary carcinoma of Cowper's gland. Surg. Gynec. Obst., 65: 238, 1937.
- HARBACH, F. O.: Primary carcinoma of the male urethra. J. Urol., 38: 311, 1937.
- HARRAH, F. W.: Primary carcinoma of the ureters. Am. J. Surg., 26: 550, 1934.
- HENNINGSEN, O.: Neue wege zur behandlung inoperabler prostatiker. Zentralb. f. Chir., 63: 2608, 1936.
- HEBST, R. H.: Papilloma of the prostatic urethra treated with radium and fulguration. Surg. Clin. North Am., 3: 1071, 1923.
- HERMAN, LEON: Practice of Urology. Phila., W. B. Saunders Co., 1938.
- HESS, E.: Bladder tumors. Urol. & Cutan. Rev., 38: 579, 1934.
- HESS, E.: Urinary hemorrhage—a symptom, not a disease, etc. Pennsylvania M. J., 39: 698, 1935-36.
- HEYMAN, JAMES: Erfahrungen mit radiologischer behandlung bei genitalkarzinom. Deutsche med. Wchnschr., 58: 367, 1932.
- HINMAN, F.: Tumors of the testis: five-year cures following radical operation. Surg. Gynec. Obst., 56: 450, 1933.
- HINMAN, F.: Principles and Practice of Urology. Phila., W. B. Saunders Co., 1935.
- HINMAN, F.: Radical operation for teratoma testis. Am. J. Surg., 28: 16, 1935.
- HINMAN, F., AND POWELL, T. O.: The management of tumor of the testis. J. A. M. A., 110: 188, January 15, 1938.
- HOED, D. DEN: Results obtained in the treatment of malignant tumors of the vagina, vulva, and urethra. Acta Radiol., 17: 569, 1936.
- HORN, K. W., AND NESBIT, R. M.: Carcinoma of the penis, with report of 37 cases. Ann. Surg., 100: 480, 1934.
- HYMAN, A.: Clinical study of malignant tumors of the kidney. Surg. Clin. North Am., 13: 347, 1933.
- KEYES, E. L.: Five-year results of suprapubic radium implantation. Surg. Gynec. Obst., 58: 233, 1934.

- KEYES, E. L., AND FERGUSON, R. S.: Roentgenotherapy for recurring bladder tumors of low malignancy. *Trans. Am. Assoc. Genito-Urinary Surg.*, 28: 265, 1935.
- KIDD, F.: Treatment of bladder tumors by radon. *Brit. M. J.*, 2: 949, 1930.
- KIRWIN, T. J.: Chorionepithelioma of the testicle: case report. *J. Urol.*, 38: 91, 1937.
- KIRWIN, T. J.: Primary epithelioma of the male urethra. *J. Urol.*, 27: 539, 1932.
- KIRWIN, T. J.: Instruments for the measurement and radon implantation of urologic lesions. *J. Urol.*, 38: 194, 1937.
- KIRWIN, T. J.: The management of bladder tumors. *Surg. Gynec. Obst.*, 66: 998, June 1938.
- LECOMTE, R. M.: The management of renal tumors, including cysts. *J. A. M. A.*, 105: 1963, 1935.
- LEIGHTON, W. E.: Cancer of the penis, with report of 67 cases. *Am. J. Cancer*, 16: 251, 1932.
- LEWIS, L. G.: Young's radical operation for cure of carcinoma of the penis: report of 34 cases. *J. Urol.*, 26: 295, 1931.
- LOWER, W. E.: The standard treatment of malignant tumors of the bladder. *Surg. Gynec. Obst.*, 60: 513, 1935.
- LOWSLEY, O. S., AND HUNT, R. W.: The present status of transurethral surgery. *Urol. & Cutan. Rev.*, 43: 83, February 1939.
- MOORE, R. A.: Morphology of small prostatic carcinoma. *J. Urol.*, 33: 224, 1935.
- MOORE, R. A., *et al.*: Histologic studies of effect of irradiation on benign hypertrophy of the prostate. *Trans. Am. Assoc. Genito-Urin. Surg.*, 31: 371, 1938.
- PASTEAU AND DEGRAIS: Quoted by Burnam.
- PFAHLER, G. E.: *Diagnosis and treatment of cancer of the bladder by means of the roentgen ray.* Pennsylvania M. J., May 1936.
- PFAHLER, G. E.: Diagnosis and treatment of tumors of the bladder by means of the roentgen rays. *Surg. Gynec. Obst.*, 64: 989, 1937.
- PFAHLER, G. E., AND VASTINE, J. H.: Roentgen diagnosis and treatment of tumors of the bladder . . . results of treatment by irradiation. *J. A. M. A.*, 104: 609, 1935.
- PHILIPS, H.: X-rays and radium in benign hypertrophy of the prostate. *Med. J. & Rec.*, 127: 238, 1928.
- POMEROY, L. A.: Three cases of primary carcinoma of the female urethra treated with radium. *Am. J. Obst. & Gynec.*, 27: 606, 1934.
- PORTMANN, U. V.: Measurement of radiation dosage. *Am. J. Roent.*, 21: 170, 1929.
- RANDALL, A.: Advantages of preoperative x-ray in kidney tumor in children. *Ann. Surg.*, 100: 462, 1934.
- RANDALL, A., AND BOTHE, A. E.: Value of preoperative irradiation in tumor of the testis. *Ann. Surg.*, 105: 385, 1937.
- RENTSCHLER, C. B.: Primary epithelioma of the vulva. *Ann. Surg.*, 89: 709, 1929.
- SARGENT, J. C., AND MARQUARDT, C. R.: Primary carcinoma of the ureter. *J. Urol.*, 30: 625, 1933.
- SCHILLER, V., AND ALTSCHUL, W.: Roentgenotherapie der prostatahypertrophie. *Strahlentherapie*, 36: 179, 1930.
- SCHREINER, B. F.: Treatment of epithelioma of the penis. *Radiol.*, 13: 353, 1929.
- Second Internat. Congress Radiol., Stockholm, Sweden, Report of: Standardization of roentgen dosage. *Acta Radiol., Suppl. III, Pt. 2*, pp. 226-239, 1929.
- SMITH, G. G., AND PIERSON, E. L.: Value of high-voltage x-ray therapy in carcinoma of the prostate. *J. Urol.*, 23: 331, 1930.
- SPARKS, T. P., AND PARSONS, W. H.: Carcinoma of the female urethra. *Urol. & Cutan. Rev.*, 41: 157, March 1937.

- TAUSSIG, F. J.: Leukoplakic vulvitis and cancer of the vulva. *Am. J. Obst. & Gynec*, 18: 472, 1929.
- UHLE, C. A. W., AND ARCHER, G. F.: Primary carcinoma of Cowper's glands: report of case and review of literature. *J. Urol.*, 34: 128, 1935.
- WATERS, C. A.: Preoperative irradiation of cortical renal tumors. *Am. J. Roent & Rad. Therap.*, 33: 149, 1935.
- WATERS, C. A., LEWIS, L. G., AND FRONTZ, W. A.: Radiation therapy of renal cortical neoplasms. *Southern M. J.*, 27: 290, 1934.
- WATSON, E. M.: Carcinoma of the male urethra. *J. Urol.*, 21: 207, 1929.
- WATSON, E. M.: Carcinoma of the female urethra. *J. Urol.*, 35: 654, 1936.
- WESSON, M. B.: Malignant tumors of the testicle and scrotum: their treatment with conservative surgery and deep roentgen therapy. *Am. J. Surg*, 2: 243, 1927.
- WHARTON, L. R.: Preoperative radiation of massive tumors of the kidney: clinical and pathologic study. *Arch Surg*, 30: 35, 1935.
- WHITE, G.: Use of Stent composition in radium treatment of carcinoma of the urethra and vagina. *Lancet*, 1: 1462, 1937.
- WIDMAN, B. P.: Cancer of the prostate results of radium and roentgen ray treatment. *Radiol*, 22: 153, 1934.
- YOUNG, H. H.: Radical cure of cancer of the prostate. *Surg Gynec Obst.* 64: 472 1936.

CHAPTER XL

DRIED HUMAN BLOOD PLASMA THERAPY

A decade and a half have passed since the idea of drying and storing human blood plasma was first made practical; but it was not until the outbreak of World War II that its immense therapeutic possibilities were fully realized. The first report published in this country seems to have been that of D. B. Kendrick, Jr., which appeared in *The Military Surgeon* for February, 1941. Since that time many accounts have appeared, not only in medical literature but in the lay press as well. Appeals to the general public to contribute blood for the production of plasma have greatly stimulated this interest, until the whole subject has received discussion and analysis not often accorded to purely medical matters.

PREPARATION AND PACKAGING OF DRIED PLASMA

Blood plasma is the liquid portion of the blood prevented from clotting by an anticoagulant after removal of the cellular structures. It may be dried to a powder and reconstituted by the addition of distilled water after a period as long as five years. Plasma may be used without typing, which makes it instantly available.

It is under emergency conditions—whether in peace or in war—that dried human blood plasma finds its greatest usefulness. At present, it is in combat areas—in the treatment of shock, hemorrhage, and burns—that its life-saving qualities are most dramatically being demonstrated. Under most conditions transfusion of plasma has shown itself to be equal in effectiveness to transfusion of whole blood of established compatibility, and under war conditions it is very often superior because of its ease of transportation and readiness for instant service in the most varied and trying circumstances.

In this country, a satisfactory system of collection, preparation, and packaging for shipment has been carried out by the national government, although much of the experimental work has been done in private laboratories.

A standard package consists of a fiberboard box containing two rubber-diaphragm-capped bottles of 400 cc. capacity. One bottle contains dried

plasma which has been reduced from 250 cc. of original normal plasma, or 300 cc. of citrated plasma, sealed under 29 inches of vacuum. The second hottle is filled with 300 cc. of distilled sterile water, sealed without vacuum. The hottle of dried plasma, together with the equipment for intravenous administration accompanying every plasma kit, is sealed in a tin can under 25 inches of vacuum. The hottle containing the distilled water is sealed in a tin can filled with dry nitrogen. The complete outfit is packed in a form easily transported and made ready for use, and is supplied by leading pharmaceutical houses.

An improved method of administering blood plasma is that proposed by Willcutts and Hicks, by which 6 or 8 patients can be treated from one hottle simply by closing a pinch clamp and changing the needle between patients. A satisfactory apparatus consists of a 2,000 cc. Ahhott intravenous bottle with a removable bakelite dispensing cap with slotted blood strainer attached, bakelite blood filter, Murphy drip, screw pinch cock, needle, needle adapter, three short lengths of rubber tubing, and a rubber pressure bulb. The bulb is attached to the "in" nipple of the dispensing cap, replacing the air filter which usually is fastened here; when manipulated, it serves to create positive air pressure in the hottle, forcing the plasma through the small-bore needle at any desired rate of delivery. The venoclysis tubing is fastened to the "out" nipple as in regular venoclysis. The blood filter is inserted in the venoclysis line above the Murphy drip. Administrations of plasma from one 2,000 cc. bottle can be given to as many as 6 or 8 patients merely by closing the pinch clamp and changing the needle adapter and needle between patients. The removable cap makes cleaning of the unit easy.

ADVANTAGES OF PLASMA OVER WHOLE BLOOD

The practical advantages which the use of blood plasma has over that of whole blood have been well summarized by DeBakey, speaking especially of military practice:

1. Whole blood transfusion requires a suitable donor, necessitating tests for compatibility and freedom from disease.
2. Under war conditions especially, suitable donors are seldom available for immediate use, and delay may be fatal.
3. Plasma may be prepared in advance, in large quantities, ready for instant use whenever needed.
4. Preliminary typing and compatibility tests are unnecessary because isoagglutinins are partially suppressed by pooling and are further inhibited by the patient's own blood.

5. Dried plasma can be transported anywhere without refrigeration, and is as easily prepared for use and administered as is the ordinary normal saline solution.

DANGERS OF PLASMA ADMINISTRATION

In the enthusiasm over the great benefits derived from the use of dried blood plasma, and the success which has attended its employment under a wide variety of conditions, the fact that unpleasant, or even dangerous, after-effects are possible has been almost completely overlooked. Recently, however, attention has been directed to this possibility, which, though remote, should always be taken into consideration.

So far as we are aware, the first report of this kind was that made by Polayes and Squillace, in March, 1942. Transfusion of dried human plasma in their case caused a "near fatal reaction," which was at first thought due to some fault in the preparation of the plasma. Later, however, they were able to cross-match the patient's own blood with the plasma solution, with resulting agglutination of the red cells that constituted the strongest contraindication to its use. As it is customary for the directions which accompany plasma-administration outfits to state specifically that no preliminary cross-matching is necessary, this precaution had, of course, been omitted.

A second case was more recently (January, 1943) reported by Commander Downs of the U. S. Naval Medical Corps. His patient was "doing poorly" after an emergency cholecystotomy and the case "was thought a proper one for the use of plasma." The reaction set in no more than five minutes after plasma administration was begun, with cough, cyanosis, dyspnea, and acceleration of the pulse-rate. The plasma injection was not stopped, but the patient was given epinephrine hydrochloride immediately and glucose solution when the injection was completed. After about an hour all untoward symptoms entirely disappeared. It is notable, however, that the patient was *not* in any way benefited by the plasma therapy, but responded to transfusions of whole blood which were given subsequently.

Although such reactions are apparently rare, the fact that they have occurred makes it advisable to do cross-matching when conditions permit. As the conditions under which plasma is most often employed are not likely to permit this precaution, the risk will usually have to be taken. Nevertheless, it should be avoided if possible.

BIBLIOGRAPHY

- DEBAKEY, M. Plasma bank. *Internat Med Digest*, 40: 311, 1942.
- DOWNS, T. M. Reaction to dried pooled human plasma. *U. S. Naval Med. Bull.*, 41: 189, January, 1943.
- HILL, J. M., AND MUTRHEAD, E. E. Use of desiccated plasma in urology. *J. Urol.*, 47: 387, 1942.
- JANEWAY, C. A. Medical progress war medicine, with special emphasis on use of blood substitutes. *New England J. Med.*, 225: 371, 1941.
- KENDRICK, D. B., JR. Prevention and treatment of shock in combat zone. *Military Surgeon*, 88: 97, 1941.
- KILDUFFE, R. A., AND DEBAKEY, M. : The blood bank and the technique and therapeutics of transfusions. St. Louis, C. V. Mosby Co., 1942.
- SIRUMIA, M. M., AND MCGRAW, J. J.. Blood plasma; its place in the practice of medicine, with special consideration to problems of administration. *J. A. M. A.*, 118: 427, 1942.
- WILLCUTTS, M. D., AND HICKS, R. A. An improved method for the administration of human plasma and whole blood. *U. S. Naval Med. Bull.*, 61: 213, 1943.

INDEX

In the index references to the illustrations are marked by the letters "Ill."
Unmarked references are to the text. All references are to page-numbers.

- Abscess, follicular, 12, 644, 710
 inguinolabial, 585
- Staphylococci, *Staphylococcus aureus*, 1453, 1460, 1481
 tuberculous, 1496, Ill. 1495, 1497
 prostate, 808, 809, 811, 813, 818; Ill. 808
 operative treatment of, 819, 929; Ill. 930, 931, 933
- Scrotum, 423
 incision and drainage of, 423; Ill. 423
- Seminal vesicle, 548
 treatment of, 550
- Skene's gland, 760, 761, 762, 782
- Urethra, male, 644
 treatment of, 645
- Paranephritic, 1480
- Paraurethral, 710, 711, 713
- Perinephritic, 1455, 1480, 1497, 1510
 diagnosis of, 1481, 1480
- Bladder, 1042, 1055
 arising in urachus, 1059
 kidney, 1564, 1760; Ill. 1564
 prostate, 847; Ill. 848, 849
 Skene's gland, 769
 testicle, 454, 461
- Adenoma of adrenal cortex, 1576
 bladder, 1045, 1060
 kidney, 1566
 urethra, male, 648
- Adenomyoma of vagina, 599
 vulva, 590
- Adherent clitoris, 577
 penis, 225, 230, 233
 prepuce, 225, 233
- Adrenal gland, adenoma of, 1576
 carcinoma of, 1576
 ganglioneuroma of, 1580
 hyperplasia of, 1576
 neuroblastoma of, 1579
- Amputation of penis for carcinoma, 303, 323, 656, 657
 complete, 331; Ill. 324-331
 partial, 332
- Accessory urethra, male, 626; Ill. 627
 excision of, 628, 696, Ill. 694
 urinary meatus, 628
- Acetonuria, test for, 32
- Acid ash diet (see Diet)
- Actinomycosis of bladder, 1035
 kidney, 1525, 1631; Ill. 1526
 etiology of, 1526
 treatment of, 1529
- Ureter, 1249
- Adenocarcinoma of Bartholin's gland, 590, 1740
- function, 62
- was ureters, 559; Ill. 559
- uretero-intestinal, 1324
 Coffey's technics of, 1326, 1329
 Higgin's technic of, 1330

- Anastomosis, uretero-intestinal, *Hutchins'*
 technic of, 1334
 indications for, 1123, 1133, 1324
 Jewett's method of, 1331
- Cowper's gland, 734
 ejaculatory duct, 523, 524, 525
 epididymis, 370
 female external genitalia, 571
 kidney, 1350
 penis, 226
 prostate, 792
 scrotum, 365
 seminal vesicle, 524
 spermatic cord, 373
 testicle, 367
 ureter, 1210
 urethra, female, 749
 male, 226, 610
 vas deferens, 522
- Andren's "bottle" operation for hydrocele,
 512
- Anephrogenesis, 1362
- Anesthesia, caudal (see Anesthesia, sacral)
 for children, 100, 122, 197, 217, 318, 319
 circumcision, 319
 operations upon bladder, 218, 1102
 Cowper's gland, 218, 743
 female external genitalia, 602
 kidney, 219, 1655
 penis, 217, 318, 319
 prostate, 218, 878
 scrotum and scrotal contents, 218, 486
 seminal vesicle, 218, 560
 ureter, 219, 1302
 urethra, female, 217, 781
 male, 217, 672
 vas deferens, 218, 556
 urethral instrumentation, 72, 100, 113,
 122
 general inhalation, 190, 192, 318, 319
 as supplement to regional anesthesia,
 192, 878
 in urology, discussion and summary of,
 190, 217
 intravenous, 215, 216, 217, 318
 local, for intraurethral procedures, 72, 101,
 113, 213
 local infiltration, 212, 318
 paravertebral, 208
 rectal, with avertin, 197
 sacral and parasacral, 209, 879
 care of patient after, 212
 technic of, 210
 sedative medication preliminary to, 191
 segmental peridural, 206
 spinal, 199, 878
- Aneurysm of renal artery, 1412, 1581; *III*,
 1443
 diagnosis of, 1582
 treatment of, 1583
- Angioma of epididymis, 465
 penis, 298
 renal pelvis, 1546
 urethra, male, 649
- Angulation and kinks of ureter, 136, 151,
 154, 1219, 1222, 1223, 1224,
 1294, 1627; *III*, 153
 etiology of, 1277
 treatment of, 1279
- epididymis, 384
 female external genitalia, 381, 576
 kidney, 145, 1361, 1408, *III*, 147-149
 operative treatment of, 1689
 penis, 229
 prostate, 800
- seminal vesicle, 526
 testicle, 376
 urachus, 964
 ureter, 145, 1213
 operative treatment of, 1225, 1302
 urethra, female, 751
 male, 102, 615
 vagina, 577
 vas deferens, 526
- Anorchidism, 376
- Antiperistalsis of ureter, 1228
- Anura, 7, 908, 980, 1433
 due to sulfonamide therapy, 1171
 ureteral calculus, 1267, 1270
 hemoglobinuria, 7
 postoperative, 786
- Aplasia, renal, 1371
- Arteries of bladder, 955
 Cowper's gland, 735
 epididymis, 370
 kidney, 1345, 1349, 1357
 anomalous, 1224, 1272, 1283, 1309,
 1374, 1381, 1382
 penis, 228, 356
 prostate, 796
 scrotum, 366
 seminal vesicle, 525
 testicle, 370
 ureter, 1212
 urethra, female, 750
 vas deferens, 524
- Arteriography, renal, 171
- Aschheim-Zondek test (see Hormonal test)

- Aspiration and injection of hydrocele, 471, 511
renal cyst, 1544, 1688
spermatocele, 511
Asymmetrical fused kidney (see Fused kidney)
Atonic bladder, 998, 1037
treatment of, 1088, 1160
ureter, 136, 1228, 1291, 1412
treatment of, 1293
Atresia of hymen, 578, 600
urethra, male, 616
urinary meatus, 616
vagina, 577, 581, 595, 598
Atrophy of kidney, 1371, 1416, 1486, 1487
testicle, 371, 379, 388, 409, 413, 434, 435, 473, 475
Autolysis of testicle, 410
Automatic tidal drainage of bladder, 1160
uses of, 1161
Bacteriological tests of urine, 23, 41, 42, 120
Bacteriophage therapy, 1718
of bladder, 1195, 1718
kidney, 1473, 1718
prostate, 817, 937
seminal vesicle, 546, 567
Balanitis, 256, 710, 711
erosive and gangrenous, 259, 264
treatment of, 261
Balanoposthitis, 234, 256, 710, 711
Ballottement, renal, 14
Bartholin's glands, 576, 765
abscess of, 760, 761, 762
adenocarcinoma of, 590, 1740
cysts of, 589
extirpation of, 603, 764
Bay-fond of bladder, 835, 949
Belt's approach in perineal prostatectomy, 898
operative treatment of, 1223, 1324
Bigelow lithotrite, 375, 1126
Bilharziasis, etiology of, 1031
of bladder, 118, 1030, 1050, III, 1031
treatment of, 1034
kidney, 1525
prostate, 825
ureter, 1248
Bilobate scrotum, 375
Bisection of kidney, 1684
Bladder, 943, 986, 1102
absence, congenital, of, 958
actinomycosis of, 1035
adenocarcinoma of, 1042, 1055
arising in urachus, 1059
adenoma of, 1045, 1060
aerogram of, 174, 1056, 1084
anatomy of, 946
anesthesia for operations upon, 218, 1102
anomalies, congenital, of, 957
arteries of, 955
atonic, 998, 1037, 1088, 1160
attachments of, 946
automatic tidal drainage of, 1160
bacteriophage therapy of, 1195, 1718
bas fond of, 835, 949
bilharziasis of, 118, 1030, 1034, 1050, III, 1031
blood supply of, 955
calculus (see Calculus)
carcinoma of (see Carcinoma)
cord, 1086, 1087, 1088, 1135, 1160
cystoscopic appearance of, in disease, 116
inspection of, 115
decompression, gradual, 883, 1159
diet in treatment of, 1006, 1007, 1008, 1187, 1198
diseases of, 994, 1092
diverticulum of, (see Diverticulum)
drainage, suprapubic, of, 1150, III, 1150, 1153
duplication of, 958
echinococcus infestation of, 1035
operative treatment of, 1123, 1324
fibroma of, 1047
fistula of, 118, 994, 1076, Plate VII
communicating with bowel, 1077
uterus, 1079
vagina, 581, 756, 994, 1076
operative treatment of, 1128, 1324, III, 1130-1134
foreign body in, 117, 1075
removal of, 1075, 1124; III, 1074
fulguration of (see Fulguration)
follow-up after surgery of, 1157
gangrene of, 999, 1008, 1010
gonorrhea of, 761, 1022; III, 1022, 1023
gumma of, 1023, 1025, 1026
hemangioma of, 1048, 1093
herniation of, 1061
hour-glass, 959
leiomysoma of, 1047
leukoplakia of, 116, 1019, 1021, 1041, 1117; Plate II
localized submucous fibrosis of, 1013, 1018, 1113
37,

- Bladder, neurogenic abnormalities of, 978,
979, 1085, 1161
treatment of, 1088
- palpation and percussion of, 15
papilloma and papillomatosis of, 118,
1039, 1050, 1051, 1057, 1060,
1146, Ill. 1040; Plate IV
paralytic, 1086, 1087, 1088
physiology of, 968, 974
postoperative care following surgery of,
1116, 1149
complications of, 1149
preoperative preparation for surgery of,
1102
pressure, measurement of, 81, 978
prolapse, in female, 1064
purpura of, 117
quartz light irradiation of interior of, 1199;
Ill. 1199
radiotherapy of tumors of, 1057, 1110,
1147, 1750, Ill. 1111, 1148, 1753,
1754, 1757
radium and x-ray burns of, 993
reimplantation of ureter into, 1303, 1316,
1318, Ill. 1319
rhabdomyoma of, 1047
rupture of, 118, 179, 182, 918, 988, Ill.
989
operative treatment of, 1120
sarcoma of, 1038, 1039, 1046, 1050, 1055,
1057, 1093
sphincter, 614, 793, 906, 945, 952, 968,
971, 976, 979
subarachnoid injection of alcohol for pain
in, 1195
sympathectomy for relief of pain in, 1134
syphilis of, 117, 1023
- tumors of (see Tumors)
vaccine therapy of, 1195
varices of, 117
veins of, 956
wall, resection of for diverticulum, 1111;
Ill. 1113-1120
Hunner's ulcer, 1113
leukoplakia, 1117
tumor, 1106; Ill. 1107-1111
structure of, 948
wounds of, 986
operative treatment of, 988, 1120
- Blasucci ureteral catheter, 85
Blood chemistry, relation of, to urinalysis, 52
tests, 52
importance of, in urology, 53
securing specimens for, 61
- Blood plasma, dried human, 1766
advantages of, over whole blood, 1767
dangers of, 1768
preparation and packaging of, 1766
- Blood supply of bladder, 955
Cowper's gland, 735
epididymis, 370
kidney, 1345, 1349, 1356
anomalies of, 1224, 1272, 1279, 1280,
1283, 1309, 1374, 1381, 1382,
1409; Ill. 1280, 1410
- penis, 228
prostate, 796
scrotum, 366
seminal vesicle, 525
testicle, 370
ureter, 1212
urethra, female, 750
vas deferens, 524
- Bone formation in penis, 295, 296
Bougies, urethral, 71, 661
technic of passing, 73
- Bowman's capsule, 1345, 1348, 1349, 1354,
1355
- Brake prostatectomy bag, 891
- Bright's disease, 1423
classification of, 1424
degenerative changes of, 1424
inflammatory changes of, 1424
sclerotic lesions of, 1433
treatment of, 1433
uremia in, 1436
treatment of, 1438
- Brown-Buerger cystoscope, 104
- Bubo in chancroid, 262, 264, 266
- Bulbo-urethral gland (see Cowper's gland)
- female urethroscope and infant vagio-
scope, 90, 122, 594, 756; Ill. 91-94
- Calcification of vas deferens, ampulla, and
seminal vesicle, 532, 552; Ill. 534
kidney, tuberculous, 1497, 1509
- Calcified sebaceous cysts of scrotum, 432
- Calculus, cystine, 135, 1596
of bladder, 117, 1067, 1092, 1157; Ill.
1068, 1069; Plate VI
diagnosis of, 129, 177, 1072
in diverticulum, 129, 1072; Ill. 180,
181, 1081
removal of, by cystoscopic rongeur,
1125; Ill. 1125
litholapaxy, 1072, 1126
surgery, 1073, 1124

- kidney, 5, 168, 1583; *III.* 1598, 1601
 bilateral, 1584, 1609
 diagnosis of, 127, 1603; *III.* 149, 165
 pyelography in, 168, 1605; *III.* 165, 166, 167
 due to sulfonamide therapy, 1171, 1594
 etiology of, 1584
 incidence of, 1597
 location of, 1597
 pathological renal changes in, 1599
 recurrence of, preventing, 1606, 1609
 structure and composition of, 1594
 symptoms of, 1603
 treatment of, 1606
 by bissection of kidney, 1684
 calyceal resection, 1606, 1684
 heminephrectomy, 1606
 nephrectomy, 1606
 nephrotomy, 1606, 1674; *III.* 1675-1677, 1678
 pyelotomy, 1606, 1679, *III.* 1680
 transperitoneal, 1683; *III.* 1681-1683
 prepuce, 234, 309
 prostate, 866; *III.* 129, 867
 symptoms and diagnosis of, 129, 869
 treatment of, by operation, 870, 921, 932, 1760; *III.* 934
 radiation, 1760
 scrotum, 431
 seminal vesicle, 552, *III.* 552
 ureter, 168, 1259, 1294; *III.* 1262, 1265, 1266
 diagnosis of, 1262
 by roentgenogram, 128, 168, 1264; *III.* 165, 167
 wax bulb catheter, 84, 1264; *III.* 1263
 in diverticulum, 1258, 1260, 1270
 treatment of, 1266
 expectant, 1268
 instrumental, 1268
 symptomatic, 1267
 surgical, 1269, 1320, *III.* 1321
 urethra, female, 776, 777
 treatment of, 777
 urethra, male, 103, 129, 177, 665, 667; *III.* 178
 removal of, through perineal incision, 697; *III.* 695, 696
 suprapubic incision, 698; *III.* 697, 698
 urethroscope, 667; *III.* 667
 urinary, diet in treatment of, 1189, 1192, 1194, 1611
 dissolution of, by chemical means, 1617
 due to hyperparathyroidism, 60, 1070, 1270, 1591, 1616
 etiology of, 1067, 1260, 1584
 following alkali treatment of peptic ulcers, 1591, 1613
 postoperative roentgenography in, 1610
 preoperative roentgenography in, 1324
 recurrence of, preventing, 1606, 1609
 structure and composition of, 1260, 1594
 Calyceal resection, 1606, 1684
 technic of, 1685
 Capsule, Bowman's, 1345, 1348, 1349, 1354, 1355
 Gerota's, 1351, 1480
 prostatic, 792, 793
 renal, 1349, 1351, 1353
 Carbuncle of kidney, 1453, 1456, *III.* 1455
 treatment of, 1460, 1481
 Carcinoma of adrenal cortex, 1576
 bladder, 1039, 1041, 1049, 1050, *III.* 1042-1045, 1054; Plate IV
 diagnosis of, 1053
 in diverticulum, 1049, 1059, *III.* 1112-1114
 ectrophy, 964, 1050
 treatment of, by excision, electro-resection, or fulguration, 1057, 1106, 1147, 1324, 1751, *III.* 1107-1111, 1148, 1149, 1757
 radiation, 1057, 1110, 1147, 1750, *III.* 1111, 1148, 1753, 1754, 1757
 Cowper's gland, 742
 treatment of, by operation, 743, 1743
 radiation, 743, 1743
 kidney parenchyma, 1542, 1562
 diagnosis of, 1571
 pathogenesis of, 1562
 pathology of, 1563, 1564, 1565
 treatment of, by operation, 1573, 1760
 radiation, 1573, 1760
 pelvis, 1529, 1545; *III.* 1546, 1547
 diagnosis of, 1550
 treatment of, by operation, 1552, 1758, *III.* 1325-1328
 penis 200 206. *III.* 201-201

 prostate gland, 831, 844, 1747
 biopsy of, 851; *III.* 852-855
 diagnosis of, 850
 etiology of, 844
 metastases from, 845
 pathology of, 845, 1747; *III.* 847, 848, 849
 prognosis of, 856
 relation of serum acid phosphatase to, 853
 treatment of, 498, 857, 918
 by castration, 498, 858
 estrogenic substances, 859
 radiation, 858, 1747; *III.* 1748
 supervoltage irradiation of testes, 859
 surgery, 857, 918, 920, 1747
 transurethral resection, 852, 910, 1747; *III.* 1748

Carcinoma, scrotum, 429
 treatment of, by radiation, 431, 1736
 surgery, 431, 1736
 seminal vesicle, 550
 treatment of, by radiation, 55, 1739
 surgery, 551, 1739
 spermatic cord, 464, 1739
 testicle, 454, 461
 treatment of, by radiation, 387, 462, 1737
 surgery, 461, 498, 1737, III 500, 501
 ureter, 1252
 treatment of, by radiation, 1758
 surgery, 1257, 1324, III 1325-1328
 urethra, female, 103, 769
 treatment of, by radiation, 770, 1744
 surgery, 770, 1744
 male, 650, III. 652, 653, 654, 655
 treatment of, by radiation, 656, 657, 1742
 surgery, 656, 657, 1743
 vagina, 599
 treatment of, by radiation, 599, 600, 1739
 surgery, 599, 600, 1740
 vulva, 590
 treatment of, by radiation, 591, 1739
 surgery, 591, 1740
 Caruncle of female urethra, 103, 767, 769
 treatment of, 768
 Carunculæ hymenales, 576, 598
 Castration, effects of, 391
 for prostatic carcinoma, 498, 858
 Catheterization of ejaculatory duct, 97, 101, 185, 477, 547
 technic of, 97, 563, III. 97, 98
 ureter, 83, 1715
 in children, 122, 123
 preparation for, 87
 technic of, 118
 urethra, 74
 preparation for, 77
 technic of, 78
 Catheters, ureteral, 84
 care of, 86
 indwelling, 1315, 1471, 1473, 1716
 types and sizes of, 84
 wax-bulbed, 84, 1264, III. 1263
 urethral, 74
 care of, 77
 self-retaining, 75
 types and sizes of, 74
 Cavernosis, gonorrheal, 710, 712
 indurated, 293
 tuberculous, 288
 Chancre (see Syphilis)
 Chancroid of penis, 261
 differential diagnosis of, 261, 263, 278, 283
 etiology and bacteriology of, 261
 treatment of, 264
 scrotum, 417
 vagina, 597
 vulva, 586

Chemical nephrosis, 1432

310, 319

bladder tumors in, 1092
 cystoscopy and urethroscopy in, 122
 diseases of bladder in, 1092
 Cowper's gland, 743
 kidney, 1461, 1463, 1465, 1629
 prostate, 870
 scrotal contents, 477
 seminal vesicle, vas deferens, and ejaculatory duct, 553
 ureter, 1293
 urethra, female, 777
 male, 667
 vulva, 591
 gonorrheal vulvovaginitis in, 591; III 593

C

Chorionepithelioma of testicle, 454, 455
 459; Frontispiece
 vagina, 600, 1740
 Chyluria, 28; III. 155
 Circumcision, 234, 253, 256, 297, 310
 anesthesia for, 319
 cautery, in adults, 322
 in female, 602
 technic of, 319
 Kirwin's, 319, III. 321
 Lowley's, 319; III. 320
 Clinical tests of urine, 24
 Chloridectomy, 602
 Clitoris, 571
 adherent, 577
 anomalies, congenital, of, 577
 excision of, 602
 glans of, 572
 Coffey's technics of uretero-intestinal anastomosis, 1326, 1329
 Collection of urinary specimens, 21, 118
 Concealed penis, 230
 Condyloma acuminata of female external genitalia, 587, 597
 penis, 296
 lata in female, 585, 597
 penis, 297
 scrotum, 417, 418
 Constriction of penis, 251; III. 252
 Contracture of vesical orifice, 842, 1065; III. 1066
 Contusion of kidney, 1396, 1403
 penis, 247
 scrotum, 400

- Corper's crystal violet-potato method of detecting tubercle bacilli in urine, 42
- Corpora cavernosa penis, 224, 226, 228, 229, 309, 609
- Corpus spongiosum urethrae, 224, 226, 609, 612
- Cowperitis, 737
abscess-formation in, 738
fistula following, 738
operative treatment of, 743
- Cowper's gland, 612, 732
abscess of, 713, 738, 739
anatomy of, 734
anesthesia for surgery of, 218, 743
anomalies, congenital, of, 736
blood supply of, 735
carcinoma of, 742, 743, 1743
diseases of, 737, 743
ducts of, 613, 735
embryology of, 732
extirpation of, 745
gonorrheal infection of, 737, 738
incision and drainage of, 745; Ill. 744, 745
injuries of, 736
innervation of, 736
lymphatics of, 736
non-specific infections of, 737
number and classification of, 733
operative treatment of, 743
physiology of, 736
postoperative care of, 746
retention cysts of, 740, 743
secretion of, 736
structure of, 734
tuberculosis of, 739
tumors of, 742, 1743
veins of, 736
- Creatinine, test of blood for, 60, 61
- Crista urethralis, 749
- "Crush" injuries, disturbances of kidney function following, 1444
- Cryoscopy, 66
- Cryptorchidism, 364, 369, 371, 385, 387, 476, 477
complications of, 378, 453, 467, 468, 487
hormonal treatment of, 379, 478
operative treatment of, 379, 487; Ill. 489, 490, 493
types of, 376; Ill. 377
- Cystitis, 994, 1092; Ill. 1000, Plate II
acute, 116, 998, 1004, 1005
alkaline encrusted, 999, 1011, 1050; Plate II
amebic, 1036
bacterial, 995
chronic, 32, 116, 999, 1006
cystica, 1001, 1050
diagnosis of, 1003
treatment of, 1006, 1007, 1009
- gangrenous, 999, 1008
glandular, 1001
gonorrheal, 761, 1022; Ill. 1022, 1023
granulomatosa, 999
interstitial, 998, 999, 1014, Plate II
non-bacterial, 995
panmural ulcerative, 1014
postoperative, 995
postpartum, 996
pregnancy, 996
pseudomembranous, 1002
symptoms of, 1002
treatment of, 1005
tuberculous, 1026
types of, 998
ulcerative, 116, 1002, 1014
- Cystocele, 183, 757, 1064
treatment of, 1065
- Cystography, injection, 172; Ill. 180, 181
contrast media for, 172
in female, 183
technic of, 173
uses of, 176, 1055
- Cystometer, 82, 978
Lowsley-Hunt, 82; Ill. 82
- Cystometry, 81
uses of, 978
- Cystoscopes, care of, 111
types of, 104
- Cystoscopy, 104
anesthesia for, 113
care of patient after, 122
in children, 122
indications and contraindications for, 108
instruments for, 104
care of, 111
preparation of armamentarium for, 111
of patient for, 113
technic of, with examination of upper tract, 114
- Cystostomy (see Suprapubic)
- Cystourethrography, technic of, 175
uses of, 176, 819
- Cysts, dermoid, of spermatic cord, 464
vagina, 598
vulva, 589
hydatid (see Echinococcus)
of Bartholin's gland, 589
Cowper's gland, 740, 743
treatment of, 741
hymen, 600

Cystitis, 150, 1602, 1620, 1632

1545

unilocular, 1538

calcified, 1541

contents of, 1542

diagnosis of, 1543

etiology of, 1538

treatment of, by aspiration and injection, 1544, 1688

operation, 1544, 1688

small, multiple retention, 1530, 1538

solitary (see Simple cyst)

penoscrotoperineal raphe, congenital, 240

prostate, 824, 826

prostatic utricle, congenital, 625, 825; Ill. 625

urachus, 966, 967

urethra, male, 645, 648

vagina, 598

vulva, 589

sebaceous, of scrotum, 428; Ill. 428

calcified, 432

vulva, 589

Dark field examination for syphilis, 268, 298

Dartos, 227, 365, 366, 367

Decapsulation of kidney, 1435, 1707

technic of, 1708

Decompression, gradual, of bladder, 883, 1159

Deferentitis, gonorrheal, 529

non specific, 530

Delphic fistula, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, 902, 903, 904, 905, 906, 907, 908, 909, 910, 911, 912, 913, 914, 915, 916, 917, 918, 919, 920, 921, 922, 923, 924, 925, 926, 927, 928, 929, 930, 931, 932, 933, 934, 935, 936, 937, 938, 939, 940, 941, 942, 943, 944, 945, 946, 947, 948, 949, 950, 951, 952, 953, 954, 955, 956, 957, 958, 959, 960, 961, 962, 963, 964, 965, 966, 967, 968, 969, 970, 971, 972, 973, 974, 975, 976, 977, 978, 979, 980, 981, 982, 983, 984, 985, 986, 987, 988, 989, 990, 991, 992, 993, 994, 995, 996, 997, 998, 999, 1000

vagina, 598

vulva, 589

Diacturia, test for, 32

Diet, acid ash, 1007, 1008, 1189, 1612

alkaline ash, 1006, 1192, 1314, 1614

Brady modified, 1193

as etiological factor in urinary calculus, 1584

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

Dyspareunia, 1190, 1191

urethra, in female, 759, 764, 772, 786

male, 661, 673, 676, 685, 699, 722, 746, 816

of ureter, congenital (see Megalo-ureter) due to obstruction (see Hydro-ureter)

Diphtheria of penis, 288

Diseases of bladder, 994, 1092

Cowper's gland, 737, 743

ejaculatory duct, 553

epididymis, 433, 477

female external genitalia, 581

hymen, 576, 600

kidney and renal pelvis, 1405, 1629

penis, 252

prostate gland, 806, 870

scrotum, 414

seminal vesicle, 535, 553

testicle, 433, 477

ureter, 1239, 1293

urethra, female, 757, 777

male, 637, 667

vagina, 594

vas deferens, 529, 553

vulva, 581, 591

Dislocation of penis, 251

Diverticulum of bladder, 117, 177, 958, 1080;

Plate VII

cystography in, 177, 1084; Ill. 181

diagnosis of, 1083

etiology of, 1081

operative treatment of, 1084, 1111; Ill.

1113, 1115, 1116-1120

stone in, 129, 1072; Ill. 180, 181; 1081

tumor in, 1049, 1059; Ill. 1112-1114

ureter, 170, 1220, 1224, 1237, 1294; Ill.

1238

calculus in, 1258, 1260, 1270

treatment of, 1259

urethra, female, 751, 758, 774, 776

treatment of, 759, 776, 777

urethrography in, 179

urethra, male, 102, 179, 625, 663, 665;

Ill. 182, 664

operative treatment of, 626, 665, 667,

691; Ill. 688

Dorsal slit, 234, 253, 261, 266, Ill. 254

Duplication of bladder, 958

kidney, 145, 150, 1221, 1224

operative treatment of, 1670, 1693

penis, 231; Ill. 233

ureter, 150, 1214, 1215, 1221, 1223; Ill.

146, 149, 1216-1218

operative treatment of, 1225, 1302

urethra, female, 751

male, 626

vagina, 577

Dye tests of renal function, 46, 121, 1388

Echinococcus disease of bladder, 1035

kidney, 37, 1520, 1631

diagnosis of, 1523

operative treatment of, 1524

ureter, 1250

- Ectopic kidney, 151, 1380
 anomalous blood supply of, 1381
 operative treatment of, 1683, 1694
 stone in, 1683; Ill. 167
 transperitoneal pyelotomy for, 1683;
 Ill. 1681-1683
 with crossed ureter, 150, 1219, 1380;
 Ill. 147
 and fusion, 1378; Ill. 1379
 testicle, 364, 376, 477, Ill. 494
 complications of, 378, 487
 operative treatment of, 379, 487, 493;
 Ill. 495, 496, 497, 499
 ureteral orifices, 629, 750, 1220, 1223,
 1225; Ill. 1216, 1218
 operative treatment of, 1226, 1303
- Ejaculation, 527, 629
- Ejaculatory duct, 521, 529, 536, 557, 611, 798
 anatomy of, 523, 524, 525
 anomalies, congenital, of, 526
 catheterization of, 97, 101, 185, 477, 547,
 563; Ill. 97, 98
 dilatation of, 563
 diseases of, 553
 embryology of, 361, 522, 609
 injection of, 563
 injuries of, 529
 non-operative treatment of, 562
 physiology of, 526
 stricture or occlusion of, 477, 553, 565
- Elephantiasis of penis, 283, 292, 426; Ill. 292
 scrotum, 292, 417, 424; Ill. 292
 etiology of, 424
 treatment of, 426
- vulva, 587
- Elliott treatment regulator for applying
 heat to prostate, 937
- Elsner-Braasch endoscope, 88
- Embryology of bladder, 943
 Cowper's gland, 732
 ejaculatory duct, 361, 522, 609
 epididymis, 361
 female external genitalia, 361, 569
 kidney, 1343
 pelvis, 1208, 1346
 penis, 223
 prepuce, 225
 prostate, 787; Ill. 788, 789
 scrotum, 360
 seminal vesicle, 361, 521
 spermatic cord, 363, 364
 testicle, 361
 trigonum vesicae, 944, 946
 ureter, 1208, 1346
 urethra, female, 569, 748
 male, 225, 607
 vas deferens, 361, 521
 verumontanum, 522, 609
 vagina, 570
- Embryonal adenomyosarcoma of kidney (see
 Wilms' tumor)
- Emmet's "buttonhole" operation for pro-
 lapse of urethra, 783
- Encysted hydrocele, 376, 467
- Endoscopes, 87
- Entameba histolytica infection of bladder,
 1036
- Eauresis, 623, 629, 1088
 causes of, 1089
 treatment of, 1091
- 503-505
 transplantation of vas to testicle following,
 504; Ill. 506
- Epididymis, anatomy of, 370
 anesthesia for surgery of, 218, 486
 angioma of, 465
 anomalies, congenital, of, 384
 arteries of, 370
 blood supply of, 370
 contusion of, 406, 407
 diseases of, 433, 477
 embryology of, 361
 gonorrheal infection of, 409, 436, 475,
 517, 712
 gumma of, 447
 inflammations of (see Epididymitis)
 injuries of, 405
 innervation of, 371
 lymphatics of, 373
 neuralgia of testicle and, 449
 non-operative treatment of, 517
 non-specific infections of, 438, 475, 517
 operative treatment of, 486
 palpation of, 19
 postoperative care following surgery of,
 510, 512, 516
 preoperative preparation for surgery of,
 486
 sarcoma of, 465
 syphilis of (see Syphilis)
 tuberculosis of (see Tuberculosis)
 tumors of (see Tumors)
 veins of, 371
 wounds of, 405, 407
- Epididymitis, gonorrheal, 409, 436, 475, 712,
 713
 treatment of, 438, 517
 non-specific, 438, 475
 treatment of, 440, 517
- Epididymotomy, 438, 501
 closed, technic of, 501
 open, technic of, 502
- Epididymo-vasotomy for sterility, 477, 505
 Hagner's technic of, 508; Ill. 507, 509
 indications for, 508
- Epispadias in female, 579
 treatment of, 580, 603; Ill. 604, 605
 types of, 579; Ill. 238
 male, 237
 complete, 239
 glandular, 239
 operation for, 348; Ill. 348
 operations for, 347

- Epispadias, male, penile, Young's operation for, 349, Ill. 349
surgical treatment of incontinence accompanying, 239, 350
types of, 239; Ill. 238
- Epithelioma of scrotum, 429
treatment of, by operation, 431, 1736
radiation, 431, 1736
urethra, male, 650, Ill. 652, 653, 654, 655
treatment of, by operation, 656, 1743
radiation, 656, 1742
- Erection of penis, mechanism of, 241
muscles and nerves involved in, 228, 241, 527
pathological (see Priapism)
- Erosive and gangrenous balanitis, 259, 264
treatment of, 261
- Erythrocyte sedimentation test, 67
- Examination, dark field, for syphilis, 268, 298
instrumental, 71
in children, 122
with cystoscope, 104
ureteral catheters, 83
urethral bougies, sounds, filiforms, 71
catheters, 74
urethroscope or endoscope, 87
of blood, 52, 62, 67
prostatic secretion, 18, 541, 716, 814
semen in sterility, 476
seminal vesicular secretion, 18, 541, 565, 716, 814
urine (see Urine)
physical, in urology, 11, 12
rectal, 15, 34, 813, 819, 824, 830
- Excretory urography, 138
as measure of residual urine, 171
for examination of bladder and urethra, 176, 624
in injuries to bladder, 179, 992
kidney, 1402
male urethra, 183
postoperative studies following uretero-intestinal anastomosis, 1337
intravenous method of, 138
peroral method of, 142
preparation of patient for, 141
- operative treatment of, 1122
by uretero-intestinal anastomosis, 1123, 1324
with epispadias, in female, 579, 963
male, 237, 963
- External genitalia, female, anatomy of, 571
anesthesia for surgery of, 602
anomalies, congenital, of, 381, 576
condyloma acuminata of, 587, 597
diseases of, 581
embryology of, 361, 569
injuries to, 581
operative treatment of, 602
postoperative care following surgery of, 605
preoperative preparation for surgery of, 602
radiation of tumors of, 1739
- External urethrotomy (see Urethrotomy)
- Extraperitoneal lumbar nephrectomy, 1658, 1660, Ill. 1660-1663
- Extravasation of urine in injuries to bladder, 987
prostate, 805
ureter, 1315
urethra, 635
operative treatment of, 637, 679, 684; Ill. 680, 681
- Fascia, Buck's, 226, 293, 294, 295, 358, 635
cremasteric, 366, 412
Denonvilliers', 562, 795, 893, 922
external spermatic, 366
internal spermatic, 366
perirenal, 1351, 1481, 1620
prostatic, 795
- Fehling test for sugar in urine, 31
- Fenger operation for stricture at the ureteropelvic junction, 1307; Ill. 1307, 1308
- Fetal kidney, 1372
- Fibroma of bladder, 1047
kidney, 1568
penis, 295
renal pelvis, 1546
spermatic cord, 463
testicular tunics, 465
urethra, female, 769
male, 649
vagina, 599
vulva, 589
- Fibrosis, chronic, of prostate, 921
- Filiforms, urethral, 71, 74, 661
- excision of, 691; Ill. 669, 670
urethrovaginal, 756
repair of, 784; Ill. 784, 785
vesical, 118, 994, 1076; Plate VII
vesico-enteric, 1077
vesico-uterine, 1079
vesicovaginal, 581, 756, 994, 1076
operative treatment of, 1128, 1324; Ill. 1130-1134
- Fluids, forcing of, 885, 905, 1154, 1611, 1717
method of charting intake and output of, 1154
- Foley self-retaining catheter, 76, 884, 897, 905, 916, 917, 928, 929
- Y-plasty operation for stricture at ureteropelvic junction, 1309
technic of, 1313
- Follicular abscess, 12, 644, 710
- urethritis in male, 710
- vulvitis, 583

- Foreign body in bladder, 117, 1073
 removal of, 1075, 1124; *Ill.* 1074
 urethra, male, 632
 Foreskin (see Prepuce)
 Fossa navicularis in female, 571, 576
 male, 225, 612, 613, 617, 638, 652, 708
 Fracture of penis, 249, 250
 Frei test for lymphogranuloma venereum,
 283, 597
 Frenum preputii, 225, 227

 female, 704
 prolapsed urethra in female, 783
 tumors of bladder, 1057, 1146, 1152
 penis, 333
 urethra, male, 649
 urethral polyps and granulomas in female,
 759
 ulcers of bladder, 1018, 1197
 Fuller-Freyer technic of suprapubic prosta-
 tectomy, 887; *Ill.* 888, 889, 890,
 892
 Function tests of kidney (see Tests)
 Furunculosis of vulva, 583
 Fused kidney, 150, 1373
 asymmetrical, 150, 1375; *Ill.* 147, 1376
 horseshoe form of, 150, 1373; *Ill.* 146, 147,
 1373, 1374, 1375
 containing hypernephroma, papilloma,
 stone, 1691; *Ill.* 1691-1692
 heminephrectomy in, 1670, 1690, 1691,
Ill. 1691
 operative treatment of, 1378, 1689
 retrograde pyelography in, 150, *Ill.* 146,
 1375
 unilateral, with crossed ectopy, 1378; *Ill.*
 1379
 Galatest for sugar in urine, 31
 Ganglioneuroma of adrenal gland, 1580
 Gangrene of bladder, 999, 1008, 1010
 penis, 254, 259, 419; *Ill.* 258
 scrotum, 404, 405, 419
 and penis following periurethritis,
 419, 422; *Ill.* 420
 vagina, 595
 vulva, 584
 spontaneous fulminating, of scrotum and
 penis, 419
 treatment of, 422
 Garceau ureteral catheter, 84
 Gas bacillus infection of kidney, 1517
 treatment of, 1520
 Gerota's capsule, 1351, 1480
 Glans penis, 225, 227, 228, 608
 dorsal slit of, 234, 253, 261, 266; *Ill.* 254
 Paget's disease of, 290, 301
 clitoridis, 572
 Glass tests of urine, 24
 Glomerulonephritis (see Nephritis)
 Gonorrhea, bacteriology of, 705
 complement-fixation test for, 707, 716,
 727, 765
 history of, 702
 immunology of, 707
 in female, 755, 759
 complications of, 436, 760, 761
 criteria of cure of, 765
 diagnosis of, 761
 pathology of, 760, *Ill.* 1023
 treatment of, by chemotherapy, 763,
 764
 local, 763, 764
 prophylactic, 762
 in male, 701
 complications of, 644, 710, 711
 criteria of cure of, 726
 diagnosis of, 715
 pathology of, 708, 711
 periurethral and paraurethral abscess
 in, 710, 711
 symptoms of, 712
 treatment of, 717
 local, 721
 prophylactic, 718
 systemic, 725
 with hyperpyrexia, 726, 817
 penicillin, 720, 1185
 sulfonamides, 717, 719, 722, 724,
 727, 1165, 1166, 1167
 modes of transmission of, 708
 public health and epidemiological aspects
 of, 703
 urine examination in, 39, 716
 Gonorrheal cavernositis, 710, 712
 infection of bladder, 761, 1022, *Ill.* 1022,
 1023
 Cowper's gland, 737, 738
 ejaculatory duct, 553
 epididymus, 375, 409, 436, 712, 713
 differential diagnosis of, 437
 treatment of, 438, 517
 kidney, 1512
 prostate, 710, 712, 713, 724, 806, 810,
 818
 seminal vesicle, 535, 546, 710, 712, 713,
 714
 ureter, 1246
 urethra (see Gonorrhea, in female; in
 male)
 vagina, 591, 592, 594; *Ill.* 593
 vas deferens, 529
 vulva, 585, 591
 vulvovaginitis in children, 591
 treatment of, 592; *Ill.* 593
 Granuloma inguinale in female, 586
 male, 278, 419
 differential diagnosis of, 279, 283
 treatment of, 280
 Granuloma of urethra in female, 758, 759,
 768
 ureter, 1244
 Gubernaculum testis, 363, 411, 412

- Guinea-pig inoculation test for urinary tuberculosis, 42, 1028, 1503, 1504
- Gumma, syphilitic, of bladder, 1023, 1025, 1026
- epididymis, 447
- kidney, 1514; Ill. 1513
- penis, 295
- prostate, 820
- scrotum, 418
- testicle, 446, 459, Ill. 447
- ureter, 1247
- urethra, female, 766
- male, 639
- vulva, 586, 766
- Hagner's technic of epididymo-vasotomy, 507, 508, Ill. 507, 509
- Hemangioma of bladder, 1048, 1093
- kidney, 1569
- Hematocele, 401, 458, 469, 470
- treatment of, 404
- Hematoma, extrarenal, 163; Ill. 163
- of penis, 247; Ill. 248
- scrotum, 401, 473, 513; Ill. 248
- calcified, 431
- treatment of, 404
- Hematoporphyrinuria, 10
- Hematuria, 7, 29, 35, 108
- causes of, 7
- Heminephrectomy, 1670
- in anatomically normal kidney, 1671; Ill. 1672
- double kidney, 1670, 1693
- horseshoe kidney, 1670, 1690, 1691; Ill. 1691
- indications for, 1303, 1304, 1670
- Hemoglobinuria, 10, 35
- anuria, 7
- Hemorrhagic cyst of kidney (see Cysts)
- Hermaphroditism and pseudohermaphroditism, 381, 390
- Hernia, inguinal, accompanying cryptorchidism, 378
- congenital, 364
- differentiation of, from hydrocele, 470
- Herniation of bladder, 1061
- treatment of, 1063
- testicle, 400, 401, 408
- Herpes progenitalis of penis, 287
- Hess method of orchidectomy, 498
- Higgins' technic of uretero-intestinal anastomosis, 1330
- Ilium of kidney, 1352, 1360
- History-taking in the urological case, 1
- Hodgkin's disease of penis, 283, 304
- testis, 462
- Home's glands, 792, 800, 949
- Hormonal test for early pregnancy, 43
- tumor of testis, 44, 451, 453, 459
- therapy of cryptorchidism, 379, 478
- carcinoma of prostate, 858, 859
- Hunner's ulcer in female, 1019
- hyperplasia of prostate, 393, 840, 908
- impotence, 391
- vulvovaginitis in children, 592
- Hormones of testis, 386, 388
- influence of, on testicular descent, 364, 379
- therapeutic use of, 379, 392, 478, 908
- Horseshoe kidney (see Fused kidney)
- Hour-glass bladder, 959
- Hunner's ulcer of bladder (see Localized submucous fibrosis)
- Mast content of, 400
- idiopathic, 466
- in female, 582
- infantile, 466, 470
- inguinal, 379, 467
- interstitial, 468
- of hernial sac, 468, 470
- spermatic cord, 468, 470
- tunica vaginalis testis, 413, 458, 467, 478; Ill. 467
- traumatic rupture of tunica vaginalis in, 404
- treatment of, 471, 510
- (see)
- Hydronephrosis, 1405, 1630; Ill. 1217, 1280
- 1307, 1410, 1415
- causes of, 1406
- diagnosis of, 1418
- infected, 1405, 1462
- intermittent, 1405
- pathology of, 1414
- pyelography in, 151, 1419; Ill. 153
- renal atrophy in, 1416
- serial pyelograms in, 136, 1420
- treatment of, 1420
- Hydro-ureter, 1283, 1294; Ill. 618, 1217
- etiology of, 1284
- Hymen, atresia of, 578, 600
- cysts of, 600
- development of, 571
- imperforate, 578
- tumors of, 600
- Hypernephroma of kidney, 1562, 1563, 1564
- bilateral primary, 1569
- diagnosis of, 1571
- treatment of, by radiation, 1573, 1760
- surgery, 1573, 1760

- Hyperparathyroidism in the production of
urinary stone, 60, 1070, 1270,
1591, 1616
- Hyperplasia of adrenal cortex, 1576
- prostate gland, 110, 826
- blood chemistry tests in, 53
- complications of, 835
- cystoscopic appearance of, 116, 836;
III 836, 837; Plate V
- cysto-urethrogram in, 177; III 178
- etiology of, 826; III 828, 829
- pathology of, 831; III 838, 839, 882,
883, 903, 904
- symptoms and diagnosis of, 834, 835
- treatment of, by castration, 498, 858
- hormonal therapy, 393, 840, 908
- perineal prostatectomy, 858, 881,
891; III 893-901
- roentgen radiation, 1745
- suprapubic prostatectomy, 881,
887, III 888-892
- total perineal prostatectomy, 920,
922; III 923-928
- transurethral resection, 909
- Hyperpyrexia therapy of gonorrhea, 717,
817
- sypilis, 276
- Hypertension, arterial, current theories of
mechanism of, 1441
- renal pressor substances and, 1439
- treatment of, 1442
- by surgery, 1710
- clinical results of, 1712
- urological conditions associated with,
1443, 1558
- Hypertonic bladder, 980, 1087, 1160
- Hypoplastic kidney, 1367; III 140, 1368,
1369, 1370, 1371
- treatment of, 1370
- Hypospadias in female, 578
- treatment of, 579, 603
- male, 234, 629
- chordee associated with, 335, 340, 341;
III 337
- surgical correction of, 340; III 338,
344
- etiology of, 235
- glandular, 236
- operation for, 340; III 339
- penile, 236
- operation for, 340, III 310
- penoscrotal, 236
- Lowsley three-stage operation for,
340; III 341-347
- operations for, 335
- types of, 236; III 235
- Hypotonic bladder, 980
- Imperforate anus, urethra, vagina, case of,
576; III 573-575
- hymen, 578
- urethra, male, 616
- Impotence, 310, 475, 561, 922
- Lowsley plication operation for, 312, 350;
III 351-357
- treatment of, 311, 350, 394
- Incised wound of penis, 245, III 246
- Indigo-carmin test of renal function, 49,
121, 1388
- Inguinal lymph nodes, 229
- extirpation of, in cancer of penis, 323; III
324-331
- carcinoma of urethra, female, 770, 1744
- epithelioma of scrotum, 431
- involvement of, in cancer of penis, 302,
303, 323, 334, 1735, III 304
- cancer of urethra, male, 653, 656, 1743;
III 652
- chancre, 262, 263, 264, 266
- lymphogranuloma venereum, 282, 283,
286
- in epispadias in female, 579
- operative treatment of, 603; III 604,
605
- male, 239, 350
- operative treatment of, 350
- hypospadias in female, 603
- spina bifida, 1091, 1092
- Kelly plication operation for, 1142
- Lowsley plication operation for, 1140;
III 1142, 1143
- Lowsley repair of vesical orifice for, 1137;
III 1138, 1139
- muscle transplantation operations for,
1144
- postprostatectomy plication of external
sphincter to prevent, 897, III
902
- surgery for, in male and female, 1137
- Indigo-carmin test of renal function, 49,
121, 1388
- Inguinal lymph nodes, 229
- extirpation of, in cancer of penis, 323; III
324-331
- carcinoma of urethra, female, 770, 1744
- epithelioma of scrotum, 431
- involvement of, in cancer of penis, 302,
303, 323, 334, 1735, III 304
- cancer of urethra, male, 653, 656, 1743;
III 652
- chancre, 262, 263, 264, 266
- lymphogranuloma venereum, 282, 283,
286
- penis, 215, 308
- repair of, 334
- prostate gland, 805
- renal pelvis, 1403
- scrotum, 400

- Injuries, seminal vesicle, 529
 testicle and epididymis, 405
 ureter, 170, 1232, 1412
 diagnosis of, 1236
 treatment of, 1236, 1315, 1317
 urethra, female, 755, 756
 male, 632
 operative treatment of, 679, III. 680-683
 vas deferens, 408, 529
 vulva, 581
- Innervation of bladder, 951, 952, 955, 969, 1134
 Cowper's gland, 736
 epididymis, 371
 kidney, 1359, 1708
 micturition, 969
 penis, 228, 241, 356
 prostate, 793, 798
 scrotum, 367
 seminal vesicle, 525
 testicle, 371
 ureter, 1212
 urethra, female, 750, 969
 male, 969
 vas deferens, 372, 373, 524
- Intermittent bladder irrigation, 1159
 Internal urethrotomy (see Urethrotomy)
 Interstitial cystitis, 998, 999, 1014; Plate II
 Intertrigo of vulva, 583
 Intravenous pyelography (see Excretory urography)
- Inulin test of renal function, 1387
- Irrigations of bladder, 885, 937, 1007, 1158, 1197
 intermittent, 1159
 solutions used in, 1158
 renal pelvis, 1473, 1611, 1715
 solutions used in, 1611, 1716
- Ischiocavernosus muscle, 227, 229, 241, 353, 354, 525
- Jewett's method of uretero-intestinal anastomosis, 1331
- Kaposi's disease of penis, 299
 Kelly endoscopic tube, 87
 plication operation for urinary incontinence in female, 1142
- Ketogenic diet (see Diet)
- Kidney, 1343, 1395, 1655
 abscess of, 1153, 1460, 1481; III. 1495, 1497, 1526
 operative treatment of, 1686
 absence, congenital, of, 1362
 actinomycosis of, 1525, 1631, III. 1526
 treatment of, 1529
 adenocarcinoma of, 1564, 1760, III. 1564
 adenoma of, 1566
 amyloid degeneration of, 29, 1432
 anatomy of, 1350
 anesthesia for surgery of, 219, 1655
 anomalies, congenital, of, 145, 1361, 1408; III. 147-149
 operative treatment of, 1689
 aplasia of, 1371
 arteries of, 1345, 1349, 1357
 anomalous, 1224, 1272, 1279, 1283, 1309, 1374, 1381, 1382
 atrophy of, 1371, 1416, 1486, 1487
 bacteriophage therapy of, 1473, 1718
 bilharziasis of, 1525
 bisection of, for stone, 1684
 blood supply of, 1345, 1349, 1356
 anomalies of, 1224, 1272, 1279, 1280, 1283, 1309, 1374, 1381, 1382, 1409, III. 1280, 1410
 calcification, tuberculous, of, 1497, 1509
 calculus of (see Calculus)
 capsules, fibrous and fatty, of, 1349, 1351, 1353, 1480
 carbuncle of, 1453, 1456, III. 1455
 treatment of, 1460, 1481
 carcinoma of (see Carcinoma)
 conformation of, 1356
 contusion of, 1396, 1403
 cystadenoma, malignant papillary of, 1565
 cysts of (see Cysts)
 decapsulation of, 1435, 1707, 1708
 denervation of, 1711
 diet in treatment of, 1434
 diseases of, 1405, 1629
 duplication of, 145, 150, 1221, 1224
 operative treatment of, 1679, 1699
 embryology of, 1343
 embryonal adenomyosarcoma of, 1444, 1553, 1759
 extraperitoneal lumbar exposure of, 1658, 1660; III. 1660-1663
 fibroma and fibrosarcoma of, 1568
 function of, 1384
 disturbances of, following "crush" injuries, 1444
 tests of, 46, 52, 62, 121
 fused, 150, 1373
 asymmetrical, 150, 1375; III. 147, 1376
 horseshoe form of, 150, 1373, 1691; III. 146, 147, 1373, 1374, 1375, 1691, 1692
 operative treatment of, 1378, 1670, 1689, 1690, 1691
 unilateral, with crossed ectopy, 1378; III. 1379
 gas bacillus infection of, 1517
 gonorrhea of, 1512
 gumma of, 1514; III. 1513
 hemangioma of, 1569
 hilum of, 1352, 1360
 horseshoe (see Fused)
 hypernephroma of, 1562, 1563, 1564, 1569, 1571
 treatment of, 1573, 1760
 hypertrophic or compensatory, 1369, 1372, 1381; III. 1368

- hypoplastic, 1367; Ill. 146, 1368, 1369-1370, 1371
- injuries to, 170, 1395; Ill. 169, 1397
- operative treatment of, 1695, 1698; Ill. 1696-1698
- innervation of, 1359, 1708
- leiomyoma and leiomyosarcoma of, 1568
- leukoplakia of, 1529
- lipoma and liposarcoma of, 1568
- lobulated or fetal, 1372
- lymphatics of, 1359
- "medical" diseases of (see Nephritis; Nephrosis)
- movable (see Nephroptosis)
- non-operative treatment of, 1715
- non-specific infections of, 1450, 1461, 1474
- operative treatment of, 1655
- incisions employed in, 1657
- osteoma of, 1567; Ill. 1567
- palpation of, 13
- pelvis of (see Renal pelvis)
- physiology of, 1384
- polycystic, 56, 1372, 1531, 1545, 1633; Ill. 161, 1533
- treatment of, 1537, 1686
- postoperative care following surgery of, 1669, 1679, 1685, 1686, 1689, 1713, 1715
- complications following surgery of, 1714
- preoperative preparation for surgery of, 1656
- radiation therapy of tumors of, 1553, 1560, 1569, 1758, 1759, 1760
- operative treatment of, 1695, 1698, Ill. 1696-1698
- sarcoma of, 1562, 1563, 1567, 1568, 1571
- treatment of 1572-1760
- supernumerary, 1365; Ill. 1366
- supports of, 1352, 1618
- sympathetic surgery of, 1708, 1710
- syphilis of, 1512
- tuberculosis of (see Tuberculosis)
- tumors of (see Tumors)
- typhoid infection of, 1516
- veins of, 1350, 1358
- anomalies of, 1381, 1384; Ill. 1410
- weight of, 1356
- Wilms' tumor of, 1444, 1553, 1569, 1635, 1759
- wounds of, 1398
- Kink of ureter, 1219, 1222, 1223, 1224, 1294, 1627
- etiology of, 1277
- pyelography in, 151, 1224, 1279; Ill. 153
- serial pyelogram in, 136, 154, 1279, 1627
- treatment of, 1279
- Kirwin cystoscopic rongeur, 107, 1056; Ill. 107
- lithotrite, 107; Ill. 107
- measuring instrument and radon-seed implanter, 1058, 1750, 1751; Ill. 1748, 1752-1757
- method of circumcision, 319, Ill. 321
- method of treating vesical papillomatosis by resection and cauterization with ethyl and alcohol
- CARCIN, 140
- Lacuna magna, 102, 613
- Lavage (see Irrigation)
- Learmonth's technic of presacral neurectomy, 1135
- Leiomyoma of bladder, 1047
- kidney, 1568
- spermatic cord, 464
- testicular tunics, 465
- Leiomyosarcoma of kidney, 1568
- Leucin in urine, 40
- Leukoplakia of bladder, 116, 1019, 1041; Plate II
- treatment of, 1021, 1117
- renal pelvis, 1529
- ureter, 1246, 1252
- vulva, 588
- Lewis's universal operating cystoscope, 105
- Lipoid nephrosis, 430, 1435
- Lipoma of kidney, 1568
- scrotum, 427
- spermatic cord, 427, 463
- vagina, 599
- vulva, 589
- Lipomatosis, replacement, of kidney, 1485; Ill. 1486
- Litholapaxy, 1124, 1126
- instruments for, 1126
- technic of, 1128
- Lithotrite, Bigelow, 375, 1126
- Kirwin, 107, 1126; Ill. 107
- Littre's glands, 102, 613
- Lobulated or fetal kidney, 1372
- Localized submucous fibrosis of bladder, 1013
- treatment of 1019, 1117
- cystoscopic-roentgenographic table, 97; Ill. 99
- cysto-urethroscopy, 937
- examining table, 97

- penis, 227
 prostate gland, 787, 793
 ureter, 1211
 urethra, female, 750, 769
 male, 612, 613, 614, 968, 969
- Myogenic bladder, 980
- Myoma of bladder, 1047
 urethra, female, 769
 male, 649
- Myxoma of bladder, 1047
 epididymis, 465
 renal pelvis, 1546
 spermatic cord, 464
 testicular tunics, 465
- Nephralgia, 1629
 decapsulation for, 1707
 renal sympathectomy for, 1708
- Nephrectomy, 1659
 extraperitoneal lumbar, 1658, 1660; Ill.
 1660-1663
 for tuberculosis, 1666
- 1666
 subcapsular, 1664
 transperitoneal, 1668; Ill. 1667, 1668
- Nephritis, 1423, 1514
 acute diffuse glomerular, 30, 1424
 blood chemistry tests in, 55, 59
 chronic diffuse glomerular, 1428
 classification of, 1423, 1424
 diet in, 1434
 hypertension in, 1439
 parenchymatous, 40
- 1430, 1436
- uremia in, 1431, 1436
- Nephrolithiasis (see Calculus)
- Nephropexy, *Deming method of*, 1707
 indications for, 1629
 Lowsley ribbon-gut method of, 1703; Ill.
 1701-1705, 1706
- Nephroptosis, 136, 151, 1278, 1279, 1411,
 1617, Ill. 153
 diagnosis of, 1625
 etiology of, 1619
 serial pyelography in, 1626
 treatment, non-operative, of, 1628
 by operation, 1629, 1699, 1703, 1707;
 Ill. 1701-1705, 1706
- Nephrosis, 1423, 1429
 amyloid, 29, 1432
 chemical, 1432
 diet in, 1434
 hypertension in, 1439
 lipid, 1430, 1435
 of pregnancy, 1432
 treatment of, 1433
 by renal decapsulation, 1435
 uremia in, 1435, 1438
- Nephrostomy for permanent drainage, 1673,
 1685
Neubauer's, 1673
- Ill.
 79,
 1004, 1101
 clinical types of, 1085
 cystometrograms in, 978
 treatment of, 1088
- Nitrazine test for pH of urine, 33
- Noma vulvae, 591
- Non-operative treatment of bladder, 1158
 inoperable and postoperative urogenital
 tuberculosis, 1196
 kidney, 1715
 prostate, 935
 scrotum and scrotal contents, 517
 vas deferens, seminal vesicle, and ejacu-
 latory duct, 562
- Non-protein nitrogen, tests of blood for, 59
- Non-specific infections of Cowper's gland, 737
 epididymis, 438, 475, 517
 differential diagnosis of, 439
 treatment of, 440, 517
 kidney and renal pelvis, 1450, 1461, 1474
 prostate gland, 806, 809, 818
 treatment of, 809, 816
 seminal vesicle, 535, 546
 ureter, 1239
 urethra, female, 755
 treatment of, 759
 male, 643, 717
 vas deferens, 530
- Obturator, urethral, 77
- Oliguria, 7, 29
- Ombrière's operation for hypospadias, 336
- Operative treatment of bladder, 1102
 Cowper's gland, 743
 female external genitalia, 602
 kidney, 1655
 incisions employed in, 1657
 penis, 318
 prostate, 878
 scrotum and scrotal contents, 486
 seminal vesicle, 560
 ureter, 1302
 urethra, female, 781
 male, 672
 vas deferens, 486, 556
- Orchidectomy, 461, 498, 1737
 for carcinoma of prostate, 498, 838
 torsion of testicle, 495
- Orchidopexy, 487
 authors' method of, 488; Ill. 489, 490, 493
 for ectopic testis, 495; Ill. 495, 496, 497,
 499

- Orchidopexy, indications for, 487
 Torek technic of, 490
- Orchitis, acute, 433, 434
 chronic, 433
 of mumps, 5, 434, 435, 475
 syphilitic, 446
 treatment of, 435, 517
- Organ of Giraldes, 375
- Os penis, 295, 296
- Osteoma of kidney, 1567; Ill. 1567
- Paget's disease of glans penis, 290, 301
- Palpation of bladder, 15
 epididymis, 19
 kidney, 13
 penis, 19
 rectal, 15, 54, 813, 819, 824, 850
 testicle, 19
 ureter, 15
- Papilloma of bladder, 118, 1039, 1050, 1051,
 1060, Plate IV
 treatment of, 1057, 1146
 penis, 296
 renal pelvis, 1546, 1547
 treatment of, 1552
 ureter, 1252
 treatment of, 1257, 1758
 urethra, female, 766
 male, 648
- Papillomatosis of bladder, 1039, 1050, 1051;
 Ill. 1040; Plate IV
 treatment of, 1057
 by Kirwin's method of resection and cau-
 terization with phenol and alco-
 hol, 1146
- Paradidymis, 375
- Paralytic bladder, 1086, 1087
 treatment of, 1088
- Paraphimosis, 253; Ill. 254
 gangrene caused by, 254, Ill. 258
 treatment of, 254, Ill. 255
- Paraneuritic abscess, 1480
- Paraurethral abscess, 710, 711, 713
- Pediculosis pubis, 414
- Pelouze bodies in tuberculosis, 640
- Penicillin, 939, 1181
 infections responsive to, 1185, 1520
 modes of administering, 1183
 therapy of gonorrhea, 720, 1185
- Penis, 223, 243, 318
 absence, congenital, of, 230, 615
 adherent, 225, 230, 233
 amputation of, for carcinoma, 303, 323,
 656, 657, Ill. 324-331
 anatomy of, 226
 anesthesia for surgery of, 217, 318, 319
 angioma of, 298
 anomalies, congenital, of, 229
 arteries of, 228, 356
 chancroid of, 261, 263, 278, 283
 chordee of, 335, 340, 344; Ill. 337, 338, 344
 concealed, 230
 condyloma acuminata of, 296
 condyloma lata of, 297
 constriction of, 251; Ill. 252
 confusion of, 247
 cutaneous affections of, 256, 414
 dartos of, 227
 denudation of, 250
 diphtheria of, 288
 diseases of, 252
 dislocation of, 251
 duplication of, 231; Ill. 233
 elephantiasis of, 283, 292, 426; Ill. 292
 embryology of, 223
 erection of, 241, 527
 pathological (see Priapism)
 fibroma of, 295
 gangrene of, 254, 259, 419; Ill. 258
 glans of (see Glans)
 gumma of, 295
 hematoma of, 247; Ill. 248
 herpes progenitalis of, 287
 injuries of, 245, 308, 334
 innervation of, 228, 241, 356
 integuments of, 226
 lymphatics of, 229, 323
 lymphogranulomatosis (Hodgkin's dis-
 ease) of, 283, 304
 multiple hemorrhagic sarcoma (Kaposi's
 disease) of, 299
 muscles of, 227
 operative treatment of, 318
 palpation of, 19
 papilloma of, 296
 physiology of, 241
 plastic induration (Peyronie's disease) of,
 293, 358
 postoperative care of, 322, 333
 preparation of patient for surgery of, 318,
 319, 327
- Queyrat's erythroplasia of, 289, 301
 radiation therapy of tumors of, 303, 1734
- Raphe of, 224, 225, 360, 608
 congenital cysts and canals of, 240
- Rudimentary, 230, 615
- Rupture (fracture) of, 249, 250
- Sarcoma of, 298
- Scabies of, 414
- Suspensory ligament of, 227, 335; Ill. 356
- Syphilis of (see Syphilis)
- Tuberculosis of, 279, 283, 287, 288
- Tumors of (see Tumors)
- Urticaria of, 256
- Veins of, 228, 356
- Wounds of, 245, 247; Ill. 246
- Perineal prostatectomy (see Prostatectomy)
- Perineuritic abscess, 1455, 1480, 1497, 1510
 diagnosis of, 1484, 1630
 operative treatment of, 1460, 1485, 1689
 postoperative care of, 1689
- Perinephrium, 1480

- Perineum, musculature of, 969
 raphe of, 224, 360, 608
 congenital cysts and canals of, 240
 removal of ureteral calculus through, 1322; Ill. 1321
 transplanting urethra into, after amputation of penis for cancer, 332, Ill. 329, 330, 331
- Peristalsis of ureter, 145, 1226, 1310, 1313
 Peyronie's disease of penis (see Plastic induration)
- Pezzer self-retaining catheter, 75
- pH of urine, 32, 1605
 tests for determining, 32
- Phenolsulphonphthalein test of renal function, 46, 121
- Pheochromocytoma of adrenal gland, 1580
- Phimosis, acquired, 252; Ill. 254
 treatment of, 253
 as predisposing factor in penile cancer, 300
 in preputial calculus, 309
 congenital, 232
 treatment of, 234
- Phloridzin test of renal function, 49
- Physical examination, general, 11
 of urogenital tract, 12
 tests of urine, 27
- Physiology of adrenal gland, 1575
 bladder, 968, 974
 Cowper's gland, 736
 ejaculatory duct, 526
 kidney, 1384
 micturition, 974
 penis, 241
 prostate, 801
 scrotum, 384
 seminal vesicle, 526
 testicle, 385
 ureter, 1226
 urethra, female, 753, 968
 male, 629, 968
 vas deferens, 526
- Pilcher prostatectomy bag, 891
- Plastic induration (Peyronie's disease) of penis, 293, 358
 differential diagnosis of, 295
 treatment of, 295, 358
- Pneumoperitoneum, 171
- Poggi's method of ureteral anastomosis, 1317
- Polycystic kidney, 56, 1372, 1531, 1633, Ill. 161, 1533
 diagnosis of, 1536, 1545
 etiology of, 1532
 familial occurrence of, 1532
 incidence of, 1531
 treatment of, 1537, 1686
- Polyorchidism, 376
- Polyp of ureter, 1253; Ill. 1253
 urethra, female, 758, 766
 male, 648
 vagina, 598
- Polyuria, 6, 7, 29, 50
- Postoperative anuria, 786
 care following surgery of bladder, 1116, 1149
 Cowper's gland, 746
 female external genitalia, 605
 kidney, 1669, 1679, 1683, 1686, 1689, 1713, 1715
 penis, 322, 333
 prostate, 903, 908, 917
 scrotum and scrotal contents, 494, 49, 499, 503, 510, 512, 513, 517
 transurethral resection of prostate, 917
 ureter, 1169, 1314, 1335
 ureteropelvic junction, 1314
 urethra, female, 785
 male, 699
 complications in prostatectomy, 906
 surgery of bladder, 1149
 kidney, 1714
 scrotum and scrotal contents, 517
 transurethral resection of prostate, 917
- cystitis, 995
- nephrosis in, 1432
 pyelonephritis of, 1471, 1471
 treatment of, 1479, 1716
- Preoperative preparation of patient for prostatectomy, 880, 883
 surgery of bladder, 1102
 Cowper's gland, 743
 female external genitalia, 602
 kidney, 1656
 penis, 318, 319, 327
 prostate, 880
 scrotum and scrotal contents, 486
 seminal vesicle, 560
 ureter, 1169, 1302, 1335
 urethra, female, 781
 male, 672
 vas deferens, 556, 560
 transurethral resection of prostate, 880, 911
- roentgenography in urinary calculus, 1324
- Prepuce, adherent, 225, 233
 anatomy of, 227, 228
 calculus of, 234, 309
 development of, 225
 frenum of, 225, 227
 redundant, 232, 234, 259, 261
 sebaceous glands of, 227
 sphincter of, 227
- Presacral neurectomy, indications for, 1088, 1134
 technic of, 1135

- Priapism, 305
treatment of, 308
- Prolapse of bladder in female, 1064
- ureter, 1286, 1290
- urethra, female, 103, 755, 756, 773, 777
treatment of, 774, 783
- Pronphros, 1343
- Prophylaxis, chemical, for venereal disease, 264, 718, 762
- Prostate gland, 787, 804, 878
- abscess of, 808, 809, 811, 813, 818; Ill. 808
operative treatment of, 819, 929, Ill. 930, 931, 933
- absence, congenital, of, 800
- adenocarcinoma of, 847; Ill. 848, 849
- anatomy of, 792
- anesthesia for surgery of, 218, 878
- anomalies, congenital, of, 800
- arteries of, 796
- hactenophage therapy of, 817, 937
- bilharziasis of, 825
- biopsy of, 851; Ill. 852-855
- blood supply of, 796
- calculus of (see Calculus)
- capsule of, 792, 793
- carcinoma of (see Carcinoma)
- contiguous structures of, 798
- cysts of, 824, 826
- diet in treatment of, 816, 885, 908, 938
- diseases of, 806, 870
- embryology of, 787, Ill. 788, 789
- fascial investments of, 795
- fibrosis, chronic, of, 921
- gonorrheal infection of, 710, 712, 713, 724, 806, 810, 818
- hypertrophy of (see Hyperplasia)
- injuries to, 805
- innervation of, 793, 798
- interrelation of, to testis and hypophysis, 390, 827
- lymphatics of, 797
- massage of, 18, 814, 817, 935
- microscopic structure of, 792
- musculature of, 787, 793
- non-operative treatment of, 935
- non-specific infections of, 806, 809, 818
- operative treatment of, 878
- physiology of, 801
- postoperative care following surgery of, 903, 908, 917
complications in surgery of, 906, 917
preoperative preparation for surgery of, 880, 883, 911
- pyemia, chronic, of, 920
- radiotherapy of benign hyperplasia of, 1745
tumors of, 858, 1747, Ill. 1748
- rectal palpation of, 151, 541, 813, 819, 824, 850
- secretory function of, 801
- subsidiary glands of, 792, 799
- syphilis of, 820
- transurethral resection of (see Trans-urethral)
- trichomonas vaginalis infestation of, 824
- tuberculosis of (see Tuberculosis)
- tumors of (see Tumors)
- vaccine therapy of, 817, 937
- veins of, 797
- weight of, 795
- Prostatectomy, control of hemorrhage fol-
lowing, 801, 901, 907
- perineal, 858, 881, 891
- anesthesia for, 218, 879
- Belt's approach in, 898
- plication of external sphincter following, 897; Ill. 902
- technic of, 891; Ill. 893-898, 899-902
- vasectomy preliminary to, 557, 891
- postoperative care following, 903, 908, 917
- complications of, 906, 917
- preoperative preparation for, 880, 883
- selection of patients for, and technic of, 880
- suprapubic, 881, 887
- anesthesia for, 879
- Fuller-Freyer technic of, 887; Ill. 888, 889, 890, 892
- vasectomy preliminary to, 557, 887
- total perineal, 920
- indications for, 857, 882, 920, 932
- Lowsley-Kilgore technic of, 922; Ill. 923-928
- Young's method of, 922
- Prostatitis, acute, 806; Ill. 807
- treatment of, 808
- chronic, 809
- diagnosis of, 813
- examination of prostatic fluid in, 814
- treatment of, 816, 920
- Prostatotomy for prostatic abscess, 931; Ill. 933
- calculus, 932; Ill. 934
- Prurigo of scrotum, 415
- Pruritus scroti, 416
- vulvae, 589
- Pyelography (see Excretory urography; Retrograde pyelography)
- Pyelograms, interpretation of, 143
- Pyelonephritis, 1461
- atrophic, 1466, 1470
- diagnosis of, 1468

- factors predisposing to, 1464, 1630
 hypertension in chronic, 1443
 of pregnancy, 1471, 1474, 1479, 1716
 pathology of, 1465, 1481
 treatment of, 1471, 1716
- Pyelostomy**, 1679, 1685
- Pyelotomy**, 1679
 for calculus, 1606, 1679; *Ill.* 1681
 transperitoneal, in ectopic kidney, 1683,
Ill. 1681-1683
- Pyocele**, 469, 470
- Pyonephrosis**, 1461, 1462, 1481
 factors predisposing to, 1464
 pathology of, 1466
 treatment of, 1471, 1473
- Pyrdium**, 567, 585, 1008, 1179
- Pyuria**, 28, 36
- Queyrat's erythroplasia of penis**, 289, 301
- Radiation therapy**, historical review of,
 1724
 methods of applying, 1731
 with Kirwin measuring instrument and
 radon-seed implanter, 1058, 1750,
 1751, *Ill.* 1748, 1752-1757
 of genito-urinary tract (general discussion),
 1733
 of malignant tumors of bladder, 1057,
 1110, 1147, 1730, *Ill.* 1111, 1148,
 1753, 1754, 1757
 Cowper's gland, 743, 1743
 penis, 303, 1734
 prostate, 858, 1747; *Ill.* 1748
 renal parenchyma in adults, 1573, 1760
 in children, 1560, 1759
 renal pelvis and ureter, 1553, 1560,
 1758
 scrotum, 431, 1736
 seminal vesicle and spermatic cord,
 551, 1739
 testicle, 387, 462, 1736
 urethra, female, 770, 1744
 male, 656, 657, 1742
 vagina, 599, 600, 1739
 vulva, 591, 1739
 Wilms' tumor, 1560, 1759
 of prostatic hyperplasia, 1745
- Radical removal of genital tract for tu-
 berculosis**, 510
- Radium and x-ray burns of bladder**, 993
 therapy (see **Radiation**)
- Raphe, penile**, 224, 225, 360, 608
 penoscrotoperineal, cysts and canals of,
 240
 penneal, 224, 360, 608
 scrotal, 224, 360, 376
- Reimplantation of ureter into bladder**, 1303,
 1316, 1318; *Ill.* 1319
- tests of (see Tests)**
- pelvis, anatomy of**, 1352
- du**
- embryology of**, 1208, 1346
- inflammations of (see Pyelitis. Pyelo-
 nephritis)**
- injuries of**, 1403
- irrigations of**, 1473, 1611, 1715, 1716
- leukoplakia of**, 1529
- non-specific infections of**, 1450, 1461,
 1474
- normal, pyelographic appearance of**,
 143; *Ill.* 144
- papilloma of**, 1546, 1547, 1552
- radiation therapy of tumors of**, 1553,
 1560, 1758
- resection of redundant**, 1313, 1404;
Ill. 1308
- rupture of**, 1403
- tumors of (see Tumors)**
- rickets**, 1447
 treatment of, 1449
- sympathectomy**, 1708, 1710
- Replacement lipomatosis of kidney**, 1485;
Ill. 1486
- Resectoscopes, types of**, 913, *Ill.* 913-919
- Residual urine, determination of**, 81
- excretory urography as measure of**, 171
- Retrograde pyelo-ureterography**, 112, 122,
 129
 care of patient following, 122
 complications of, 132
 contrast media for, 131
 in children, 123
 indications and contraindications for, 130
 preparation of armamentarium for, 112
 of patient for, 113
 serial method of, 133; *Ill.* 133, 134
 advantages of, 135, 154, 1420, 1626
 technic of, 135
 technic of, 131
- Rhabdomyosarcoma of prostate**, 862, 863,
 865
 spermatic cord, 464
- Ribbon gut**, 1673
 use of, for ligating friable renal pedicle
 in nephrectomy, 1664; *Ill.* 1665
 for plicating external sphincter follow-
 ing perineal prostatectomy, 897;
Ill. 902
- scrotum, amputation of**, 513
- Reensuerno skin test for chancroid**, 262
- Reflux, vesico-ureteral**, 1228

- Ribbon, gut, use of, in calyceal resection, 1684
 heminephrectomy, 1670, 1691, 1694;
 III. 1672, 1691, 1692
 nephropexy, 1703; III. 1701-1705,
 1706
 nephrotomy, 1672; III. 1675-1677,
 1678
 plication operation for impotence, 312,
 350; III. 351-357
 plication operation for incontinence
 of urine in female, 1140; III.
 1142-1143
 plication operation for incontinence
 of urine and feces in male, 1137;
 III. 1140, 1141
 repair of kidney injuries, 1698; III.
 1696-1698
repair of vesical orifice following total
perineal prostatectomy, 928; III.
927, 928
 Rickets, renal, 1447
 treatment of, 1449
 * Roentgen therapy (see Radiation)
 Roentgenograms, plain, of bladder, 129;
 III. 180
 extra-urinary abnormalities, for differen-
 tial diagnosis, 127; III. 161, 162,
 167
 genito-urinary tract, 125
 preparation of patient for, 125
 routine method of securing, 126
 kidney, 126; III. 149, 165
 prostate, 129
 ureter, 128
 urethra, male, 129
 postoperative, in urinary calculus, 1324
 preoperative, in urinary calculus, 1610
 Rotation of kidney, 1349
 abnormal, 1382
 Rudimentary penis, 230, 615
 Rupture of bladder, 118, 179, 182, 918, 988;
 III. 989
 cystography in, 182, 992
 excretory urography in, 179, 992
 operative treatment of, 992, 1120
 kidney, 170, 1395, 1399; III. 169, 1397
 diagnosis of, 1401
 operative treatment of, 1695, 1698,
 III. 1696, 1697, 1698
 penis, 249
 treatment of, 250
 renal pelvis, 1403
 testicle, 407
 tunica vaginalis in hydrocele, 404
 ureter, 170, 1232, 1315
 urethra, male, 634, 679
 operative treatment of, 637, 679, 684;
 III. 682, 683
 postoperative dilatation in, 685
 with extravasation of urine, 635
 operative treatment of, 637, 679, 684;
 III. 680, 681
 Sacral and parasacral anesthesia (see Anes-
 thesia)
- Sarcoma of bladder, 1038, 1039, 1046, 1050,
 1055, 1057, 1093
 kidney, 1562, 1563, 1567, 1568, 1571
 treatment of, by surgery and radiation,
 1573, 1760.
 penis, 298
 multiple hemorrhagic (Kaposi's dis-
 ease), 300
 prostate, 860, III. 860-862, 864
 treatment of, by surgery and radiation,
 863
 renal pelvis, 1546
 spermatic cord, 463, 464
 ureter, 1252
 urethra, female, 770
 male, 656, 668
 vagina, 600, 1740
 vulva, 591, 1740
 Scabies of scrotum and penis, 414
 Scarpa's triangle, 229, 323
 Schistosoma haematobium infestation (see
 Bilharziasis)
 Sclerotic diseases of kidney, 1433
 Scrotum *see also* *urethra*
- anesthesia for surgery of, 218, 486
 anomalies, congenital, of, 375
 arteries of, 366
 bilobate, 375
 blood supply of, 366
 calcified sebaceous cysts of, 432
 calculi and concretions of, 431
 carcinoma of, 429, 431, 1736
 chancre, syphilitic, of, 417
 chancroid of, 417
 condyloma lata of, 417, 418
 contusion of, 400
 cutaneous affections of, 256, 414
 dartos of, 365, 366, 367
 diseases of, 414
 granulo-
 granuloma inguinale of, 419
 gumma of, 418
 hematoma of, 401, 404, 431, 473; III. 248
 injuries of, 400
 innervation of, 367
 lipoma of, 427
 lymphatics of, 229, 367
 priapism of, 410
 radiation therapy of tumors of, 431, 1736
 raphe of, 224, 360, 376
 cysts and canals, congenital, of, 240
 redundant, amputation of, 513

- scabies of, 414
 sebaceous cysts of, 428; *Ill.* 428
 calcified, 432
 suspensory for support of, 519; *Ill.* 518
 syphilis of (see Syphilis)
 tumors of (see Tumors)
 veins of, 366
 wounds of, 400
 Sebaceous cysts of scrotum, 428; *Ill.* 428
 calcified, 432
 vulva, 589
- testicle, 369, 385, 386
 Seminal fluid, 525, 526
 microscopic examination of, in sterility, 476
 Seminal vesicle, 361, 529, 560
 abscess of, 548, 550
 absence, congenital, of, 526
 anatomy of, 524
 anesthesia for surgery of, 218, 560
 anomalies, congenital, of, 526
 applying heat to, methods of, 566
 arteries of, 525
 bacteriophage therapy of, 546, 567
 calcification of, 532, 552
 calculus of, 552; *Ill.* 552
 carcinoma of, 550, 551, 1739
 diseases of, 535, 553
 duct of, 523, 524, 525
 embryology of, 361, 521
 gonorrheal infection of, 535, 546, 710, 712, 713, 724
 injuries of, 529
 innervation of, 525
 lymphatics of, 525
 massage of, 546, 564
 operative treatment of, 560
 physiology of, 526
 preoperative preparation for surgery of, 560
 radiation therapy of tumors of, 551, 1739
 rectal palpation of, 17, 541
 secretion of, 525, 526
 examination of, 18, 541, 565, 716, 814
 stripping of, 18, 541, 546, 566
 syphilis of, 547
 tuberculosis of (see Tuberculosis)
 tumors of (see Tumors)
 vaccine treatment of, 546, 567
 veins of, 525
 Seminal vesiculectomy, 510, 561
 technic of, 561
 Seminal vesiculitis, 535
 clinical forms of, 538; *Ill.* 542, 543
 diagnosis of, 540
 differential diagnosis of, 545
 gonorrheal, 535, 546, 710, 712, 713, 724
 pathology of, 536
 treatment of, 546, 562
 Seminal vesiculography, 185; *Ill.* 539, 542, 543
 after-care following, 187
 indications for, 185, 477, 545, 550
 technic of, 186
 Seminal vesiculotomy, 560
 technic of, 561
 Seminoma of testicle, 451, 453
 Serial pyelo-ureterography, 133; *Ill.* 133, 134
 advantages of, 135, 154, 1420, 1626
 technic of, 135
 Seven-glass test of urine, 26
 Simple cyst of kidney (see Cysts)
 Sims' operation for vesicovaginal fistula, 1129
 Sinus epididymis, 366
 pocularis (see Utricle, prostatic)
 renalis, 1352
 Skene's gland, 750, 756, 757, 758
 abscess of, 760, 761, 762, 782
 adenocarcinoma of, 769
 electrocauterization of, 782
 excision of, 782; *Ill.* 882
 Smegma preputii, 227, 234, 253, 309, *Ill.* 254
 Smithwick's method of splanchnic resection, 1711
 Sodium hypobromite test for quantitative estimation of urea, 51
 Solitary kidney, congenital, 1362; *Ill.* 1363
 treatment of, 1365
 cyst of kidney (see Cysts)
 Sounds, urethral, 71, 661
 technic of passing, 73
 Specific gravity of urine, 30, 50
 Spermatheca, anatomy of, 373
 anesthesia for surgery of, 218, 486
 dermoid cysts of, 464
 embryology of, 363, 364
 fibroma of, 463
 hydrocele of, 468, 470
 leiomyoma of, 464
 lipoma of, 427, 463
 lymphangioma of, 464
 operative treatment of, 486
 preoperative preparation for surgery of, 486
 sarcoma of, 463, 464
 torsion of, 411, 413, 487
 orchidectomy for, 495
 tumors of (see Tumors)
 Spermatocoele, 445, 473
 fluid, 474
 treatment of, by aspiration and injection, 511
 extirpation, 513, *Ill.* 514, 515
 Sphincter, external (urethral), 614, 793, 897, 902, 968, 973, 976, 979
 plication of, following perineal prosta-

- Spina bifida, incontinence of urine in, 1091, 1092
- Spinal anesthesia (see Anesthesia)
- Splanchnic resection for arterial hypertension, 1711
- Spontaneous fulminating gangrene of scrotum and penis, 419
- Staining urinary specimens, 38, 39
- Staphylococcus focal infection of renal cortex, 1453, 1481, 1630
- diagnosis of, 1458
- treatment of, 1460
- Stedman motor suction pump, 1152; Ill. 1153
- Stenosis of ureteropelvic junction (see Stricture)
- ureterovesical orifice, 151, 1219, 1220, 1272, 1284, 1294, 1296
- treatment of, 1269, 1276, 1277
- by operation, 1304; Ill. 1305
- urinary meatus, female, 751, 752, 755
- male, 617, 663, 673
- vagina, 598
- Sterility in male, causes of, 475
- epididymo-vasotomy for, 505, 508; Ill. 507, 509
- microscopic study of semen in, 476
- treatment of, 477, 505
- Streptococcal balanopreputial intertrigo, 257
- serial pyelogram in, 135
- sex and age incidence of, 1271
- symptoms of, 1277
- treatment of, by dilatation, 1276
- surgery, 1277
- ureteropelvic junction, 1282; Ill. 153
- associated with anomalous renal blood vessels, 1280, 1309
- diagnosis of, 1282, 1309
- operative treatment of, 1283, 1305, 1311; Ill. 1307, 1308
- ureterovesical orifice, 151, 1219, 1220, 1272, 1284, 1294, 1296
- treatment of, 1269, 1276, 1277, 1304; Ill. 1305
- urethra, female, 183, 771
- congenital, 751, 752, 771
- semile, 772
- treatment of, 753, 772, 773
- urethra, male, 103, 657, 918
- congenital, 13, 617, 638
- etiology of, 640, 657, 712
- spasmodic, 657
- treatment of, by dilatation, 661, 673
- electrosurgery, 678
- external urethrotomy, 662, 667, 675
- internal urethrotomy, 662, 674
- resection, 676; Ill. 677, 678
- urinary meatus, in female, 751, 752, 755
- male, 617, 663, 673
- vas deferens, 475, 477, 532
- Stripping of seminal vesicle, 18, 541, 546, 566
- Stylets, ureteral, 85
- urethral, 77
- Subarachnoid injection of alcohol for bladder pain, 1195
- Subcapsular nephrectomy, 1664
- Subcervical glands (of Albarran), 792, 799, 831, 842, 934
- Subcutaneous excretory urography, 141
- Subtotal and total paravertebral sympathectomy for arterial hypertension, 1712
- general rules for therapy with, 1174
- in treatment of chancroid, 266
- cystitis, 1006, 1007, 1012
- gonorrhea in female, 763
- male, 717, 719, 722, 724, 727
- gonorrheal vulvovaginitis in children, 592
- method of determining concentration of, in blood and other tissue fluids, 1175
- mode of action of, 1163
- pharmacology of, 1163
- renal obstruction due to crystalline deposits in therapy with, 1171
- toxic complications of, 1170
- use of, in preoperative preparation and postoperative care in uretero-intestinal anastomosis, 1169, 1335, 1336
- in prophylaxis against gonorrhea and chancroid, 719
- Supernumerary kidney, 1365; Ill. 1366
- testicle, 376

- Suprapubic cystostomy, 1105, 1150
 preliminary to prostatectomy, 883, 886, 891
 technic of, 886, 1105; Ill. 1103, 1104
 lithotomy, 1125
 prostatectomy (see Prostatectomy)
 suction cup, 1151; Ill. 1151, 1152
 drainage, 1150, Ill. 1150, 1153
- Syphilis, 266
 chancre (primacy lesion) of, 266
 in urethra, female, 765
 male, 637, 638, 765
 vagina, 597
 on penis, 266, 301; Ill. 277
 differential diagnosis of, 259, 263, 270, 279, 283, 415
 scrotum, 417
 vulva, 585
 dark field examination in, 268, 298
 determining freedom from, 276
 etiology of, 267
 of bladder, 117, 1023
 kidney, 1512, Ill. 1513
 penis, 266, 295, 297; Ill. 277
 prostate, 820
 scrotum, 417, 418
 seminal vesicle, 547
 testicle and epididymis, 445, 459, Ill. 447
 ureter, 1247
 urethra, female, 763
 male, 637
 vagina, 597
 vas deferens, 532
 vulva, 585
 treatment of, 270
 drugs used in, 271
 general requirements of, 273
 with hyperpyrexia and chemotherapy, 276
 Wassermann test in, 268
- Tabetic bladder, 1135; Ill. 989, Plate III
 Teratoma of testicle, 44, 451, 453, 459, 461, 498, 1736; Ill. 454, 453
- Test, Albarran's experimental polyuria, 50
 Ambard's excretion-retention, of renal function, 62
 McLean's modification of, 62
 Benedict's, for sugar in urine, 31
 complement-fixation, for echinococcus renal disease, 1523
 gonorrhea, 707, 716, 727, 765
 Corper's crystal-violet-potato, for tubercle bacilli in urine, 42
 erythrocyte sedimentation, 67
 Fehling's, for sugar in urine, 31
 for acetoneuria, 32
 diaceturia, 32
 Frei, for lymphogranuloma venereum, 293, 597
 Galatest, for sugar in urine, 31
 guinea-pig, for urinary tuberculosis, 42, 1028, 1503, 1504
 heat and acetic acid, for albumin in urine, 30
 hormonal, for early pregnancy, 43
 tumor of testicle, 44, 451, 453, 459
 indigo-carmin, of renal function, 49, 121, 1388
 intradermal, for echinococcus renal disease, 1524
 inulin, of renal function, 1387
 Koranyi's cryoscopy, of renal function, 66
 methylene blue, of renal function, 48
 Mosenthal diet, of renal function, 49
 nitrazine, for pH of urine, 33
 phenolsulphonphthalein, of renal function, 46, 121
 phloridzin, of renal function, 49
 precipitin, for renal echinococcus disease, 1523
 Reconstituted skin, for chancroid, 262
 seven-glass, of urine, 26
 three-glass, of urine, 24
 two-glass, of urine, 24
 urea-clearance, 64
 urease, for urea nitrogen, 52, 57
 urine-concentration, 52
 urine dilution, 52
 Wassermann, 268
- Urea, 64
 non-protein nitrogen, 59
 urea nitrogen, 57, 64
 of renal function, combined excretion-retention, 62
 excretion, 46, 121
 retention, 52
 of urine, animal inoculation, 42
 bacteriological, 23, 41, 42, 120
 chemical, 30
 clinical, 24
 glass, 24
 microscopic, 35
 physical, 27
- Testicle, absence, congenital, of, 376
 adenocarcinoma of, 454, 461
 anatomy of, 367
 anesthesia for surgery of, 218, 486
 anomalies, congenital, of, 376
 arteries of, 370
 atrophy of, 371, 379, 388, 409, 413, 434, 435, 473, 475
 autolysis of, 410
 blood supply of, 370
 carcinoma of, 454, 461, 498, 1736
 chorionepithelioma of, 454, 455, 459; Frontispiece
 contusion of, 405, 407
 descent of, 363
 influence of hormones on, 364, 379, 478
 diseases of, 433, 477
 ectopic, 364, 376, 477; Ill. 494
 operative treatment of, 379, 487, 493; Ill. 495-499

- testicle and epididymis, 440, 477, III 442
 differential diagnosis of, 444
 etiology of, 440, 482
 treatment of, 445, 502, 510, III 503-505
- ureter, 1151, 1497
 operative treatment of, 1324, 1366, III 1325-1328
- urography in, 155, 1251; III 158
- urethra, female, 766
 male, 639
 treatment of, 641
- urinary tract, culturing urine for, 42, 1503, 1504
 diet in treatment of, 1193, 1198
 erythrocyte sedimentation test in, 67
 guinea-pig inoculation test for, 42, 1028, 1503, 1504
 staining urinary specimens in, 37, 1508
- vagina, 596
- vas deferens, 532, III 531
- vulva, 585
- radical removal of genital tract for, 510
- treatment of inoperable and postoperative urogenital, 1196
 constitutional, 1197
 urological, 1196
 with quartz-light irradiation, 1198, 1199
 with tuberculin, 1198
- Tuberculous meningitis, 1511
- Tumors of adrenal gland, cortical, 1575
 operative treatment of, 1578
- medullary, 1579
 operative treatment of, 1581
- bladder, 1037, 1157
 age and sex incidence of, 1050
 benign, 118, 1038, 1039, 1045, 1046, 1055
 classification of, 1038
 cystogram and aerogram in, 174, 1054
 cystoscopic appearances of, 1053; Plate IV
 diagnosis of, 1053
 etiology of, 1050
 in children, 1092
 in diverticulum, 1049, 1059; III 1112-1114
 malignant, 9, 118, 1038, 1041, 1048, 1049, 1751; III 1040, 1042-1045, 1054
 metastasis, extension and recurrence in, 1049
 originating in urachus, 1059
 securing biopsy specimen of, 1036
 with Kirwin rongeur, 107; III 107
 Lowley rongeur, 106; III 106
 treatment of, by fulguration, excision, or electroresection, 1037, 1057, 1106, 1146, 1147, 1324, 1751, 1752; III 1107-1111, 1148, 1149, 1757
 by radiotherapy, 1057, 1110, 1147, 1850; III 1111, 1148, 1753, 1754, 1757
- Cowper's gland, 742
 treatment of, by operation and radiation, 743, 1743
- epididymis, 445
- penis, benign, 296
 malignant, 298, III 301-304
 differential diagnosis of, 279, 283, 299
 treatment of, by amputation of penis, 303, 323; III 324-331
 fulguration, 333, 1735
 radiation, 303, 1734
- prostate, malignant, 831, 844, 860, 1747; III 847-849, 861-863, 864
 biopsy of, 851; III 852-855
 treatment of, 498, 857, 865, 918
 by castration, 498, 858
 estrogenic substances, 859
 radiation, 858, 865, 1747, III 1748
 supravoltage irradiation of testes, 859
 surgery, 857, 865, 918, 920, 1747
 transurethral resection, 852, 910, 1747, III 1748
- renal parenchyma, 1561
 bilateral primary malignant, 1569
 diagnosis of, 1571
 hypertension in, 1444, 1558
 in adults, 1561; III 1564
 histopathology of, 1562
 pathogenesis of, 1562
 treatment of, by operation, 1573, 1760
 radiation, 1573, 1760
 in children, 1444, 1553
 treatment of, by operation, 1559
 radiation, 1560, 1759
- pyelography in, 159, 1571, III 162, 163
- transpantoneal nephrectomy for, 1663, III 1667, 1668
- renal pelvis, 1545, III 1546, 1547
 diagnosis of, 1550
 histopathology of, 1546
- treatment of, by surgery and radiation, 431, 1736
- seminal vesicle, 550
 treatment of, by operation and radiation, 550, 551, 1739
- spermatic cord, benign, 463
 malignant, 464
 treatment of, 464, 1739
- testicle, 368, 445, 451; III 454, 455
 benign, 452
 classification of, 453
 diagnosis of, 456, 458
 etiology of, 452
 hormonal test for, 44, 451, 453, 459
 treatment of, by operation, 461, 498
 1736; III 500, 501
 radiation, 387, 462, 1736

- Tumors, testicular tunics, 465**
 urachus, 1039
 ureter, benign, 1232
 malignant, 1252
 treatment of, 1257, 1324, 1758, III.
 1325-1328
 urethra, female, 103, 769
 benign, 766
 malignant, 769
 treatment of, by operation, 770, 1744
 radiation, 770, 1744
 urethra, male, 103, 648
 benign, 648
 treatment of, 649
 malignant, 650, 656, III 652, 653, 654,
 655
 treatment of, by operation, 656, 657,
 1743
 radiation, 656, 657, 1742
 vagina, benign, 598
 malignant, 599
 treatment of, by operation and radia-
 tion, 599, 600, 1739
 vulva, benign, 589
 malignant, 590
 treatment of, by operation and radia-
 tion, 591, 1739
 Wilms', 1553, 1558, 1569, 1635
 treatment of, by operation, 1559
 radiation, 1560, 1759
Tunica albuginea, 226, 361, 367, 370, 408,
498
 tumors of, 465
 vaginatus, 364, 366, 370, 373
 hydrocele of, 413, 458, 467, 478, III. 467
 treatment of, 510, 511, 512
 traumatic rupture of, in hydrocele, 404
 tumors of, 465
Two-glass test of urine, 24
Typhoid infection of kidney, 1516
Tyrosin in urine, 40

Undescended testicle (see Cryptorchidism)
Urachus, 616, 944, 964
 cyst of, 966, 967
 fistula of, 965, 967
 patent, 964, 967
 tumors of, 1039

 anatomy of, 1040
 anesthesia for surgery of, 219, 1302
 anomalies, congenital, of, 145, 1213
 operative treatment of, 1225, 1302
 antiperistalsis of, 1228
 arteries of, 1212
 atonic, 136, 1228, 1291, 1293, 1412
 bifurcation of, 150, 1214, 1215, 1221, 1224,
 1257; III. 149, 1366
 operative treatment of, 1225, 1302
 bilharziasis of, 1248
 blood supply of, 1212
 calculus of (see Calculus)
 carcinoma of, 1252
 treatment of, 1257, 1324, 1758; III.
 1325-1328
 catheterization of, 83, 87, 118, 122, 123,
 1715
 dilatation, congenital, of (see Megalo-
 ureter)
 diverticulum of, 1248
 ectopic orifices of, 629, 750, 1220, 1223,
 1225; III. 1216, 1218
 operative treatment of, 1226, 1303
 embryology of, 1208, 1346
 fistula of, 1234, 1235, 1237, 1269
 gonorrhea of, 1246
 granuloma of, 1244
 gumma of, 1247
 injuries of, 170, 1232, 1236, 1412
 treatment of, 1238, 1315, 1316
 innervation of, 1212
 kinks and angulations of, 136, 151, 154,
 1219, 1222, 1223, 1224, 1277,
 1294, 1627; III. 153
 treatment of, 1279
 leukoplakia of, 1246, 1252
 lymphatics of, 1212, 1452
 musculature of, 1211
 non-specific infections of, 1239
 obstructions of, 1270
 operative treatment of, 1302
 palpation of, 15
 papilloma of, 1252, 1257, 1758
 peristalsis of, 145, 1226, 1310, 1313
 physiology of, 1226
 polyps of, 1253; III. 1253
 postoperative care following surgery of,
 1169, 1314, 1335
 preoperative preparation for surgery of,
 1302
 prolapse of, 1286, 1290
 stricture of (see Stricture)
 syphilis of, 1247

- transplantation of, into intestine (see Anastomosis, uretero-intestinal)
- triplication of, 1218
- tuberculosis of (see Tuberculosis)
- tumors of, 1252, 1257
- veins of, 1212
- wall of, structure of, 1211
- wounds of, 1232
- Ureterectomy, 1324, 1667, 1669
with removal of bladder wall surrounding ureteral orifice, 1324; *Ill.* 1325-1328
- Ureteritis, gonorrheal, 1246
non-specific, 1239
granulosa, 1244
- Ureteritis cystica, 1240, 1244; *Ill.* 1242, 1243
- Ureterocele, 118, 1220, 1285, 1294; *Ill.* 1217; Plate VI
etiology of, 1286
treatment of, 1289
by fulguration, 1290, *Ill.* 1287
- Uretero-intestinal anastomosis (see Anastomosis)
- Ureterolithotomy, 1269, 1270, 1320
perineal, 1321; *Ill.* 1321
vaginal, 1323
- Ureteroneocystotomy, 1303
- Ureteropelvic junction, non-calculous obstructions of, 1279
diagnosis of, 1282, 1309, 1313
due to aberrant renal vessels, 1224, 1272, 1279, 1280, 1283, 1309, 1312; *Ill.* 1280, 1410
fibrous bands or adhesions, 1272, 1279, 1410
high insertion of ureter, 1282, 1309, 1311
hypertrophy of ring muscle, 1309
stricture, 1282, 1283, 1305, 1309
operative treatment of, 1283, 1305
by Fenger procedure, 1307; *Ill.* 1307, 1309
Foley Y-plasty, 1309, 1311, 1313
Ramstedt procedure, 1309
ureteropyeloneostomy, 1311, 1312, 1313
prolonged nephrostomy drainage and ureteral splinting in, 1311, 1312
postoperative care following plastic surgery for, 1314
symptoms of, 1282
- Ureteropyeloneostomy, 1311, 1312, 1313
- Ureterovesical orifice, 1211, 1228, 1291
enlargement of, by fulguration or cystoscopic scissors, 1269, 1277
stenosis of, 151, 1219, 1220, 1272, 1284, 1294, 1296
treatment of, 1269, 1276, 1277, 1304; *Ill.* 1305
- Urethra, female, 748, 755, 781
absence, congenital, of, 751
anatomy of, 749
anesthesia for surgery of, 217, 781
anomalies, congenital, of, 751
arteries of, 750
calculus of, 776, 777
carcinoma of, 103, 769
treatment of, 770, 1744
caruncle of, 103, 767, 770
chancre, syphilitic of, 765
crista urethralis of, 749
crypts of, 750
dilatation, instrumental, of, 759, 764, 772, 777
diseases of, 757, 777
diverticulum of (see Diverticulum)
duplication and bifurcation of, 751
ectopic ureteral orifices in, 752, 777
embryology of, 569, 748
fibroma of, 769
fistula of, communicating with vagina, 786
repair of, 784; *Ill.* 784, 785
glands of, 749, 750, 755, 756, 757, 758, 760
gonorrheal infection of, 755, 759
granulomas of, 758, 759, 768
injuries of, 755, 756
innervation of, 750, 769
lacunae of, 757, 758
lymphatics of, 615, 750
meatus of, 750, 765, 771, 773
stenosis of, 751, 752, 755
musculature of, 750, 769
myoma of, 769
non-specific infections of, 755, 759
operative treatment of, 781
papilloma of, 766
physiology of, 753, 968
polyps of, 753, 759, 766
postoperative care following surgery of, 785
preoperative preparation for surgery of, 781
prolapse of, 103, 755, 756, 773, 777, 783
sarcoma of, 770
stricture of (see Stricture)
tuberculosis of, 766
tumors of (see Tumors)
urethrography in lesions of, 183, 772, 775, 776
urethroscopic appearance of, 103
valves, congenital, of, 752, 777
veins of, 750
- Urethra, male, 607, 632, 672
abscess of, 644, 645
absence, congenital, of, 615
accessory, 626, *Ill.* 627
excision of, 628, 696; *Ill.* 694
adenoma of, 648
anatomy of, 226, 610
anesthesia for surgery of, 217, 672
angioma of, 649
anomalies, congenital, of, 102, 615
atresia of, 616
burns of, 633
calculus of (see Calculus)
carcinoma of (see Carcinoma)
catheterization of, 74, 77, 78

- Urethra, chancre, syphilitic, of, 637, 638
 cylindrical syphiloma of, 638
 cyst of, 645, 648
 dilatation, instrumental, of, 661, 673, 676,
 685, 699, 722, 746, 816
 diseases of, 637, 667
 diverticulum of (see Diverticulum)
 duplication of, 625
 ectopic ureteral openings into, 629
 embryology of, 225, 607
 epithelioma of, 650, 656, 1742, III. 652,
 653, 654, 655
 examination of, with bougies, sounds, etc.,
 71
 fibroma of, 649
 fistula of, 647; III. 647
 communicating with perineum, 738, 740
 excision of, 691, 693, III. 689, 690
 communicating with rectum, repair of,
 694; III. 691-693
 foreign body in, 632
 glands of, 613, 614, 644, 709, 710, 711, 722
 gonorrheal infection of, 701
 gumma of, 639
 imperforate, 616
 injuries of, 632
 operative treatment of, 679; III. 680,
 681, 682, 683
 innervation of, 969
 lacuna magna of, 102, 613
 lymphatics of, 325, 613
 meatus of, 226, 613, 663, 673
 accessory, 628
 atresia of, 616
 stenosis of, 617, 663, 673
 musculature of, 612, 613, 614, 968, 969
 myoma of, 649
 non specific infections of, 643, 717
 operative treatment of, 672
 papilloma of, 648
 physiology of, 629, 968
 polyps of, 648
 postoperative care of, 699
 preoperative preparation for surgery of,
 672
 prostatic-duct openings into, 610, 792
 rupture of, 634, 679
 operative treatment of, 637, 679, 684,
 III. 680-683
 sarcoma of, 656, 668
 sphincter, external, of, 614
 stricture of (see Stricture)
 syphilis of, 637
 trichomonas vaginalis infestation of, 641
 tuberculosis of, 639
 tumors of (see Tumors)
 urethrograms in study of, 172, 176; III.
 178
 urethroscopic appearance of, 101
 examination of, 87
 valves, congenital, of posterior, 617, 618,
 1284, III. 618, 619, 622
 treatment of, 624, 685
 with resectoscope, 686; III. 686, 687
 wounds of, 632
- Urethritis, gonorrheal, in female, 755 759
 male, 701
 non-specific, in female, 755, 757
 male, 643, 717
 Urethrocele, 756, 774
 treatment of, 776
 Urethrography, injection, 172
 contrast media for, 172
 in female, 183
 technic of, 175
 uses of, 176
 Urethrorhineal fistula (see Fistula)
 Urethrosopes and cysto-urethrosopes, care
 of, 111
 types of, 87
 Urethroscopy, 87
 anesthesia for, 100
 in children, 122
 indications for, 100
 instruments for, 87, 122
 preparation for, 100
 technic of, 101
 Urethrotome, Maisonneuve, 674
 Otis, 674
 Urethrotomy, external, 662, 667
 technics of, 675, 676
 internal, 662, 773
 technic of, 674
 Urethrovaginal fistula (see Fistula)
 Urinary antiseptics, 1162, 1177
 in cystitis, 1006, 1007
 kidney infections, 1471, 1472, 1611
 neurogenic vesical dysfunction, 1088
 Urination (see Micturition)
 Urine, acetone in, 32
 albumin in, tests for, 30
 animal inoculation tests of, 42
 bacteria in, 37
 bacteriological tests of, 23, 41, 42, 120
 Benedict's test for sugar in, 31
 blood in (see Hematuria)
 casts in, 40
 chemical tests of, 30
 chyle in, 28
 clinical tests of, 24
 color of, 27
 collecting specimens of, 21
 from individual kidney, 118
 concentration test, 52
 connective tissue fibers in, 36
 crystals in, 28, 35, 40
 due to sulfatherapy, 1171
 cystine in, 29, 40
 diacetic acid in, 32
 dilution test, 52
 diversion of, in urogenital surgery, 334,
 637, 781, 786
 epithelial cells in, 36
 examining unstained specimen of, 39
 extraneous structures in, 41
 extravasation of (see Extravasation)
 fat globules in, 40
 Fehling's test for sugar in, 31
 Galatest for sugar in, 31
 glass tests of, 24

- hydrogen-ion concentration of (see pH)
 incontinence of (see Incontinence)
 leucin in, 40
 microscopic examination of, 23, 25, 35, 120
 odor of, 29
 organized sediments in, 40
 parasites and ova in, 28, 37
 pH of, 32, 120
 methods of determining, 33
 physical tests of, 27
 preservatives for, 22
 quantity of, 29
 reaction of, 32
 residual, 81, 171
 shreds in, 29
 specific gravity of, 30, 50
 staining specimens of, 37, 38, 120
 sugar in, tests for, 30
 tyrosin in, 40
 unorganized sediments in, 39
 urea nitrogen in, tests of, 51, 120
 Urography (see Excretory; Retrograde)
 Urological examining and treatment tables, 96
 case history, 1
 Urticaria of penis, 256
Urethral stricture (see Stricture)
- Vaccine therapy of bladder, 1195
 gonorrhea, 725
 kidney, 1473
 prostatitis, 817, 937
 seminal vesiculitis, 546, 567
 Vagina, absence of, 577
 adenomyoma of, 599
 anomalies, congenital, of, 577
 atresia of, 577, 581, 595, 598
 carcinoma of, 599, 1740
 chancroid of, 597
 chorionepithelioma of, 600, 1740
 condyloma acuminata of, 597
 condyloma lata of, 597
 cysts of, 598
 diseases of, 594
 duplication of, 577
 embryology of, 570
 fibroma of, 599
 gangrene of, 595
 gonorrheal infection of, 591, 592, 594, III
 593
 inflammations of, 594
 injuries of, 581
 lipoma of, 599
 lymphogranuloma venereum of, 597
 polyps of, 598
 radiation therapy of tumors of, 599, 1739
 removal of ureteral calculus through,
 1323
 sarcoma of, 600, 1740
 stenosis of, 598
 syphilis of, 597
 trichomonas vaginalis infestation of, 595,
 596
 tuberculosis of, 596
 tumors of (see Tumors)
 Vaginismus, 598, 600
 Vaginitis, 594
 treatment of, 595
 Valves, congenital, of posterior urethra, 102,
 617, 618, 1284, III 618, 619, 622
 diagnosis of, 623
 etiology of, 621
 in female, 752, 777
 treatment of, 624, 685
 with resectoscope, 685; III 686, 687
 Varices of bladder, 117
 vulva, 582
 Varicocele, 371, 471
 treatment of, 472, 514
 by injection, 515
 operation, 516
 Vancoclectomy, 516
 Vas deferens, 373, 521, 529, 556
 ampulla of, 521, 523, 525
 calcification of, 532; III 534
 anastomosis of, 559, III 559
 anatomy of, 522
 anesthesia for surgery of, 218, 556
 anomalies, congenital, of, 526
 arteries of, 524
 diseases of, 529, 553
 embryology of, 361, 521
 gonorrheal infection of, 529
 injuries of, 408, 529
 innervation of, 372, 373, 524
 lymphatics of, 373
 non-operative treatment of, 562
 non-specific infection of, 530
 operative treatment of, 486, 556
 palpation of, 19
 physiology of, 526
 preoperative preparation for surgery of,
 556, 560
 structure or occlusion of, 475, 477, 532
 syphilis of, 532
 transplantation of, to skin of groin follow-
 ing removal of testis
- III 534
 tuberculosis of (see Tuberculosis)
 vas puncture, 566
 Vasectomy, 557
 preliminary to prostatectomy, 557, 887,
 891
 transurethral resection, 911
 technic of, 557; III 558
 Vasotomy, 556, 566
 technic of, 557
 Veins of bladder, 936
 Cowper's gland, 736
 epididymis, 371
 kidney, 1350, 1358
 anomalous, 1381, 1383; III 1410
 penis, 228, 356
 prostate, 797
 scrotum, 366
 seminal vesicle, 525